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Artificial Molecular-Level Machines: Which Energy To Make Them Work?[†]

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ABSTRACT

The concept of machine can be extended to the molecular level by designing and synthesizing (supra)molecular species capable of performing mechanical movements. The energy needed to make a machine work can be supplied as chemical energy, electrical energy, or light. When a chemical "fuel" is used, waste products are formed, whereas this is not the case when suitable photochemical or electrochemical energy inputs are employed. A number of elementary functions performed by molecular-level machines are illustrated, and more complex ones are foreseen.

1. Introduction

The concept of a machine can be extended to the molecular level.[1] A *molecular-level machine* can be defined as an assembly of a discrete number of molecular components designed to perform mechanical-like movements (output) as a consequence of appropriate external stimuli (input).

The extension of the concept of a machine to the molecular level is important not only for basic research but also for the growth of nanoscience and nanotechnology. The miniaturization of components for the construction of useful devices, which is an essential feature of modern technology, is currently pursued by a large-downward (top-down) approach. This approach, however, which leads physicists and engineers to manipulate progressively smaller pieces of matter, has its intrinsic limitations. An alternative and promising strategy is offered by the small-upward (bottom-up) approach. Chemists are already at the bottom, since they are able to manipulate molecules (i.e., the smallest entities with distinct shapes and properties) and are therefore in the ideal position to develop bottom-up strategies for the construction of nanoscale machines.

It has long been known that our body can be viewed as a very complex ensemble of molecular-level machines that power our motions, repair damage, and orchestrate our inner worlds of sense, emotion, and thought. The idea of constructing artificial molecular-level machines, however, is quite recent. This topic was briefly discussed for the first time by Richard P. Feynman,[2] Nobel Laureate in Physics, in his famous address, "There's Plenty of Room at the Bottom", to the American Physical Society in 1959, and only in the past few years have systematic studies been performed in this field.[1]

2. Characteristics of Artificial Molecular-Level Machines

Molecular-level machines operate via electronic and nuclear rearrangements, i.e., through some kind of chemical reaction. Like macroscopic machines, they are characterized by (i) the kind of energy input supplied to make them work, (ii) the kind of movement performed by their components, (iii) the way in which their operation can be controlled and monitored, (iv) the possibility to repeat the operation at will, (v) the time scale needed to complete a cycle of operation, and (vi) the function performed.

The problem of the energy supply to make artificial molecular-machine work [point (i)] will be discussed in detail in the next section. Here we will briefly comment on the other requirements. The motions performed by the component parts [point (ii)] may imply rotations around covalent bonds or the making and breaking of intercomponent noncovalent bonds. To control and monitor the machine operation [point (iii)], the motions of the component parts should cause readable changes in some properties of the system; any kind of chemical or physical techniques can be useful, particularly the various types of spectroscopies. Since a machine has to work by repeating cycles [point (iv)], an important requirement is that any chemical reaction taking place in the device has to be reversible. The operation time scale [point (v)] can range from less than picoseconds to hours, depending on the nature of the molecular components and the type of rearrangements involved. Finally, the functions that can be performed by exploiting the movements of the components in artificial molecular-level machines [point (vi)] are various and, to a large extent, still unpredictable.

3. Energy Supply

To make a machine work, energy inputs have to be supplied [point (i) above]. The most obvious way to supply

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energy to a chemical system is through an exergonic chemical reaction. In his address to the American Physical Society, R. P. Feynman observed,[2] "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 machines that sustain life.

If a molecular-level machine works by inputs of chemical energy,[3] 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 machine unless they are removed from the system, as 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-level machines based on "chemical fuel" inputs.

Chemical fuel, however, is not the only means by which energy can be supplied. Nature shows that in green plants the energy needed to sustain the machinery of life is provided by sunlight. Furthermore, humans have invented a great variety of macroscopic machines powered by electrical energy. Photochemical and electrochemical energy inputs can, indeed, cause the occurrence of *endergonic* chemical reactions, which can make a machine work without formation of waste products. Currently there is an increasing interest in the development of photon- and electron/hole-powered molecular-level machines, taking advantage of the recent, outstanding progress made in supramolecular photochemistry[4] and electrochemistry.[5] In the case of photoexcitation, the most likely candidates are photoisomerization[6] and photoinduced redox reactions. In the case of electrochemical inputs, the induced processes are, of course, redox reactions. Needless to say, the operation of a molecular machine is accompanied by partial conversion of free energy into heat, regardless of the chemical, photochemical, and electrochemical nature of the energy input.

Photochemical and electrochemical energy inputs offer other advantages compared to chemical energy inputs. For example, they can be switched on and off easily and rapidly. It should also be noted that electrodes represent one of the best ways to interface molecular-level systems with the macroscopic world, and lasers provide the opportunity of working in very small space and very short time domains. A further advantage offered by the use of photochemical and electrochemical techniques is that photons[4] and electrons,[5] besides supplying the energy needed to make a machine work, can also be useful to "read" the state of the system and thus to control and monitor the operation of the machine.

In this Account, we illustrate a few examples of chemically, electrochemically, and photochemically driven molecular-level machines developed in collaboration with the group of Professor J. F. Stoddart and investigated in our laboratory.

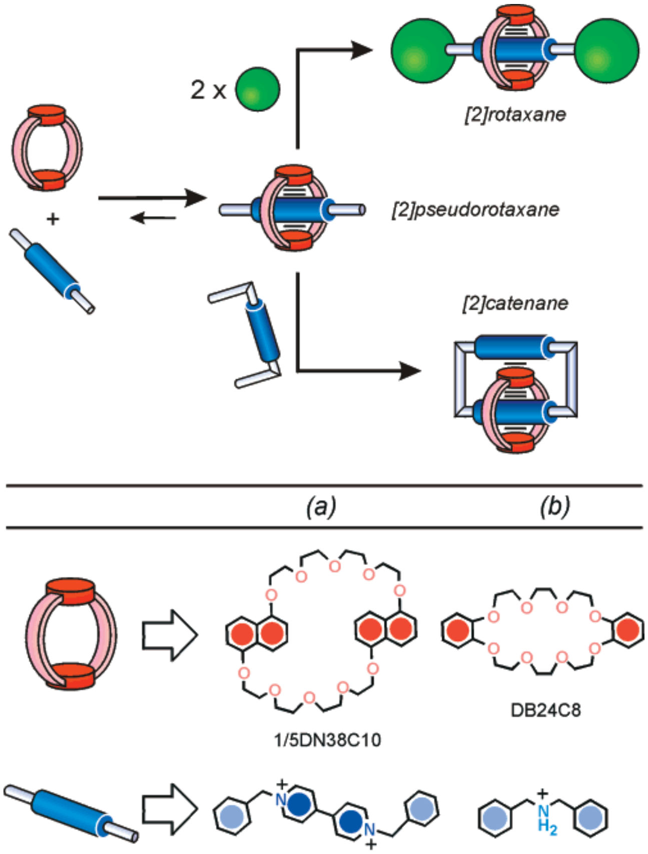

FIGURE 1. Pictorial representation of the self-assembly of pseudorotaxanes based on (a) CT and C—H···O hydrogen-bonding interactions and (b) N^+—H···O hydrogen-bonding interactions. A possible route toward the synthesis of rotaxanes and catenanes is also schematized.

4. Pseudorotaxanes, Rotaxanes, and Catenanes

Since the molecular-level machines discussed in this Account are based on pseudorotaxanes, rotaxanes, and catenanes, we will briefly recall some relevant features of these multicomponent systems. The strategies chosen by Stoddart and co-workers (Figure 1)[7] are based on (i) charge-transfer (CT) and C—H···O hydrogen-bonding interactions between an electron acceptor (e.g., 1,1′-dibenzyl-4,4′-bipyridinium dication) and an electron donor (e.g., 1,5-dinaphtho[38]crown-10, hereafter indicated by 1/5DN38C10), and/or (ii) hydrogen-bonding interactions between secondary ammonium functions (e.g., dibenzylammonium ion) and a suitable crown ether (e.g., dibenzo[24]crown-8, hereafter indicated by DB24C8).

CT interactions between electron-donor and electron-acceptor units have important consequences from the spectroscopic and electrochemical viewpoints.[1c] Namely, they imply the presence of low-energy CT excited states, which are responsible for the broad and weak absorption bands in the visible region, and for the quenching of the potentially luminescent excited states localized on the molecular components (Figure 2a). Furthermore, such interactions induce changes in the potential values of some redox processes and, for catenanes, also changes

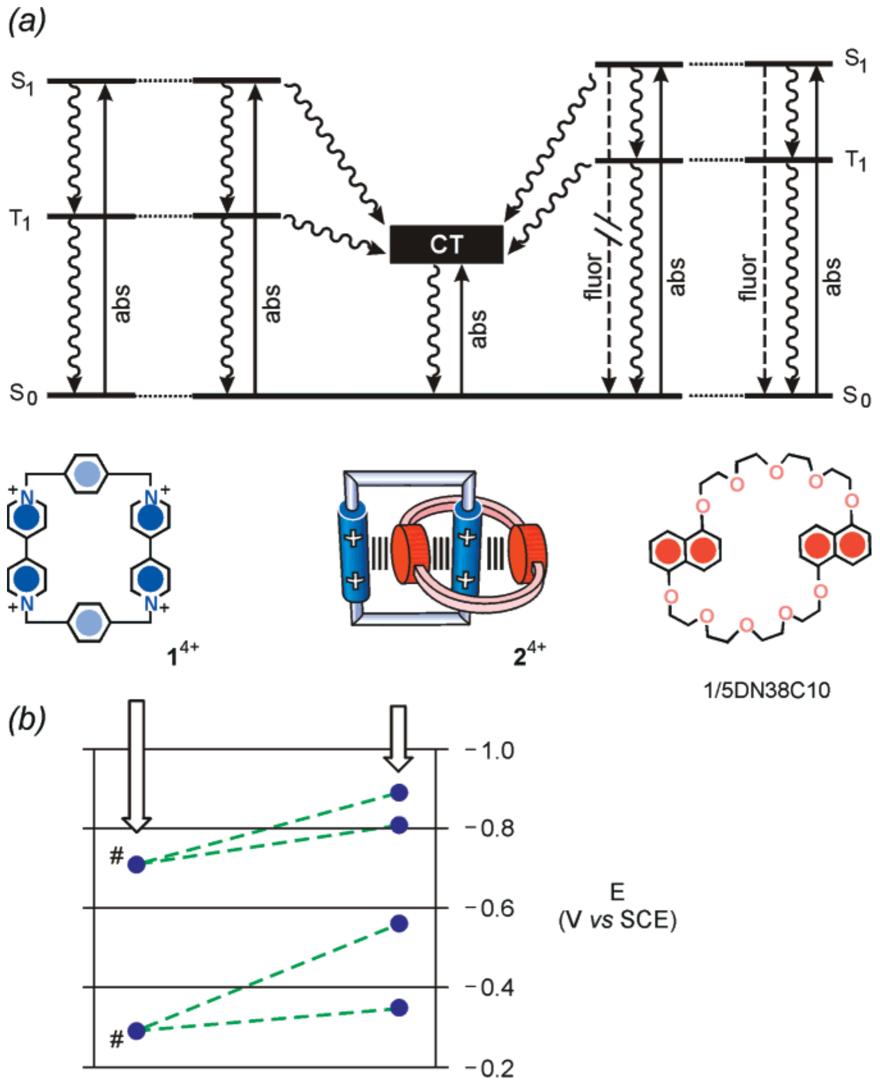

FIGURE 2. (a) Schematic energy level diagram for a catenane based on CT interactions and for its separated components; the wavy lines indicate nonradiative decay paths of the electronic excited states. (b) Correlations between the reduction potentials of the electron acceptor cyclophane **1**$^{4+}$ and its catenane **2**$^{4+}$; processes marked with # involve two electrons (MeCN, room temperature).

in the redox patterns (Figure 2b). In pseudorotaxanes, rotaxanes, and catenanes based on CT interactions, mechanical movements can be obtained by reducing the electron-acceptor unit(s) or oxidizing the electron-donor unit(s). In most cases, the CT interactions can be restored by opposite redox processes, which thus promote reverse mechanical movements leading back to the original structures. The redox processes needed to cause the mechanical movements can be obtained by chemical, photochemical, and electrochemical inputs.

Contrary to what happens in the case of CT interactions, hydrogen-bonding interactions (Figure 1b) do not introduce low-lying energy levels and do not cause strong changes in the electrochemical behavior of the molecular components. In this case, mechanical movements can be driven by acid/base inputs that create/destroy the hydrogen-bonding interactions which are responsible for assembly and spatial organization. The easiest way to produce an acid/base input is the addition of suitable chemical species, but photochemical and electrochemical inputs can also be used in principle.

By a suitable design, different types of intercomponent interactions (e.g., charge transfer and hydrogen bonding) can be present in the same system. This possibility opens the way to the construction of machines in which the interplay of different stimuli causes complex mechanical movements that can be exploited for obtaining valuable functions.

5. Molecular Machines Powered by Chemical Fuels

5.1. A Plug/Socket Device. Chemical energy inputs can be used to control threading/dethreading processes in pseudorotaxanes. This simple mechanical movement can be exploited to design systems capable of performing interesting molecular-level functions.[8] Figure 3 illustrates the case of a system that may be considered as a molecular-level plug/socket device.[9] The plug-in function is based on the threading of a (±)-binaphthocrown ether by a (9-anthracenyl)benzylammonium ion. The association process can be reversed quantitatively (plug out) by

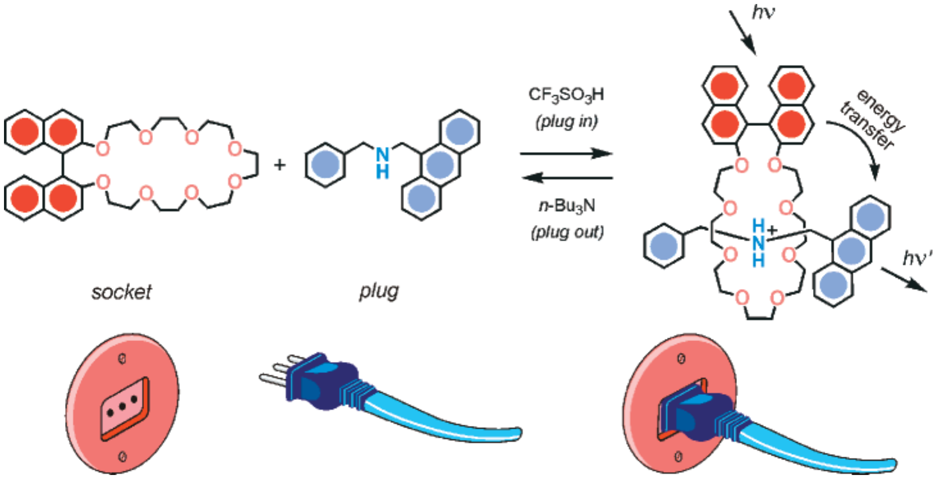

FIGURE 3. A molecular-level plug/socket device: "plug in/plug out" is acid/base controlled, and photoinduced energy transfer takes place in the "plug in" state (CH_2Cl_2, room temperature).

addition of a suitable base such as tributylamine. In the plug-in state (pseudorotaxane), an energy-transfer process takes place, as evidenced by the quenching of the binaphthyl fluorescence, which is accompanied by the sensitization of the fluorescence of the anthracenyl unit linked to the ammonium ion. As a consequence of the reversibility of the acid/base reactions, the energy-transfer process can be switched on and off at will.

The plug/socket molecular-level concept can be extended to stereoselective systems, construction of molecular-scale extensions,[10] and design of systems where light excitation induces an electron flow instead of an energy flow.

5.2. A Controllable Molecular Shuttle. In rotaxanes containing two different recognition sites in the dumbbell component, it is possible to switch the position of the ring between the two "stations" by an external stimulus.[11] A system which behaves as a chemically controllable molecular abacus is shown in Figure 4. It is made of a DB24C8 macrocycle and a dumbbell component containing a dialkylammonium center and a 4,4′-bipyridinium unit. An anthracene moiety is used as a stopper because its absorption, luminescence, and redox properties are useful for monitoring the state of the system. Since the hydrogen-bonding interactions between the DB24C8 macrocycle and the ammonium center are much stronger than the CT interaction of the macrocycle with the bipyridinium unit, the stable isomer is that in which the macrocycle surrounds the ammonium station. Upon deprotonation, displacement of the macrocycle to the bipyridinium unit is obtained. The switching process is fully reversible. This system could be useful for information processing since it exhibits a binary logic behavior.[12] It should also be noted that, in the deprotonated rotaxane, the crown can be displaced from the bipyridinium station by destroying the CT interactions through reduction of the bipyridinium or oxidation of the crown. It follows that in this system the mechanical movements can be induced by two different types of stimuli (acid/base and electron/hole), which is an interesting possibility for future developments.

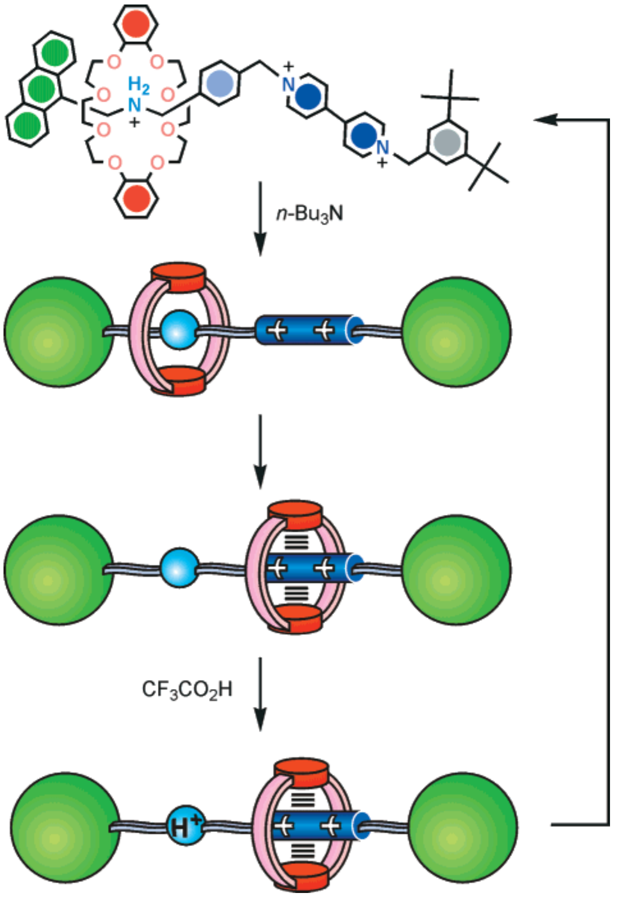

FIGURE 4. A chemically controllable molecular shuttle: the ring can be switched between the two "stations" of the dumbbell component by base/acid inputs (MeCN, room temperature).

6. Molecular Machines Powered by Electrochemical Energy

6.1. Controllable Ring Motions in Catenanes. In the catenane shown in Figure 5,[13] the electron acceptor tetracationic cyclophane $\mathbf{1}^{4+}$ is "symmetric", whereas the other ring contains two different electron-donor units, namely, a tetrathiafulvalene (TTF) and a 1,5-dioxynaphthalene (DN) unit. The TTF unit, which is the better

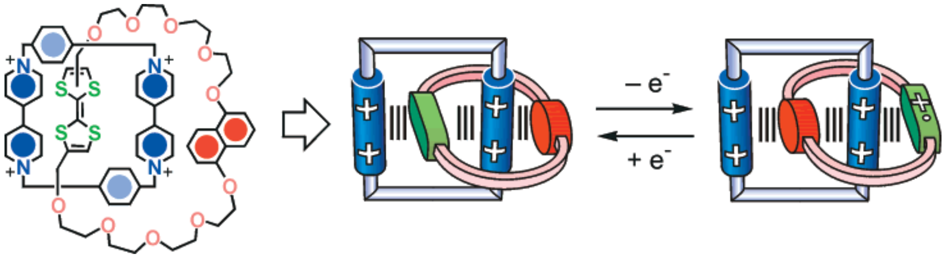

FIGURE 5. Electrochemically controlled movements upon one-electron oxidation/reduction of a TTF unit in a catenane containing a nonsymmetric ring (MeCN, room temperature).

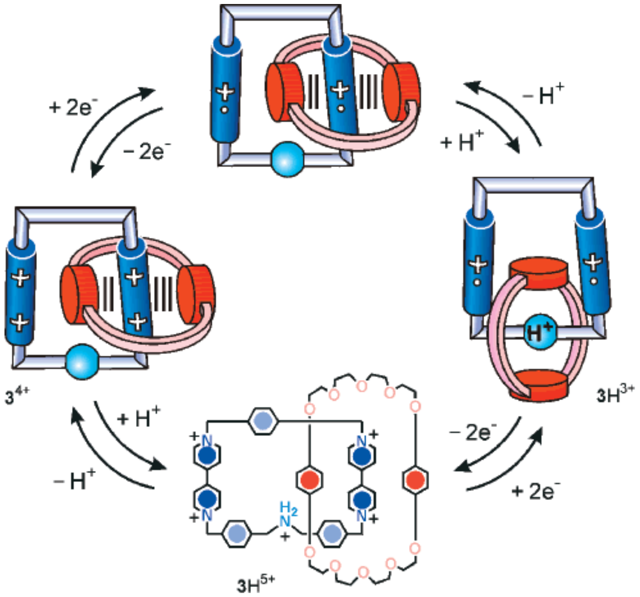

FIGURE 6. Switching processes of catenane **3**H^{5+} (MeCN, room temperature). Starting from catenane $\mathbf{3}^{4+}$, the position of the macrocyclic polyether switches under acid/base and redox inputs according to an AND logic.

electron donor, occupies the inside position where it can interact with both of the electron-acceptor units, whereas the DN unit remains alongside. On electrochemical oxidation, the first process involves TTF, which thus loses its electron-donating properties. Furthermore, an electrostatic repulsion arises between TTF^{+} and the surrounding tetracationic macrocycle. These effects cause circumrotation of one ring to yield the conformation in which the DN moiety is positioned inside the electron acceptor cyclophane (Figure 5). Upon reduction of TTF^{+}, the initial conformation is restored. This catenane has recently been used to construct a solid-state electronic device.[14]

We have recently examined[15] the behavior of catenane **3**H^{5+} shown in Figure 6. The absorption spectra and electrochemical properties show that the macrocyclic polyether surrounds a bipyridinium unit both in **3**H^{5+} and in its deprotonated form $\mathbf{3}^{4+}$, indicating that protonation/deprotonation does not cause any displacement of the macrocycle.[16] Electrochemical measurements show that, after one-electron reduction of both of the bipyridinium units of **3**H^{5+}, the macrocycle is displaced on the ammonium function, which means that an electrochemically induced conformational switching does occur. Furthermore, upon deprotonation of the two-electron reduced form **3**H^{3+}, the macrocyclic polyether moves to one of the monoreduced bipyridinium units. Therefore, $\mathbf{3}^{4+}$ behaves according to an AND logic, a function associated with two energy inputs of different nature.

6.2. Controllable Movements in Pseudorotaxanes and Rotaxanes. Electrochemical inputs can also be used to control threading/dethreading in pseudorotaxanes and ring shuttling in rotaxanes.[1,5] These topics cannot be discussed here for space reasons.

7. Molecular Machines Powered by Light Energy

7.1. Photochemically Driven Piston/Cylinder Systems. Dethreading/rethreading of the wire and ring components of a pseudorotaxane resembles the movement of a piston in a cylinder. In systems which are primarily stabilized by electron donor–acceptor interactions, like that formed by the tetracationic cyclophane $\mathbf{1}^{4+}$ and the threadlike species **4** containing a 1,5-dioxynaphthalene unit (Figure 7),[17] CT absorption bands appear in the visible region of the spectrum. Light excitation in these bands leads formally to the transfer of an electron from the donor to the acceptor component and is therefore expected to destabilize the CT interaction responsible for self-assembly. This simple approach to photoinduced dethreading, however, is precluded by the fact that the back electron transfer, that is, the deactivation of the CT excited state to the ground state, is much faster than the separation of the molecular components, a process which requires extended nuclear motions. In some particular cases,[18] laser flash photolysis experiments have been interpreted as indicating the dissociation of a small fraction of the irradiated complex.

To achieve a consistent light-induced dethreading of the pseudorotaxane structure, a different approach was devised[17] (Figure 8a). In deaerated solutions, irradiation with visible light of an external electron-transfer photosensitizer **P** (e.g., $[Ru(bpy)_3]^{2+}$) causes reduction of one of the bipyridinium units of the ring while the back-electron-transfer reaction is prevented by the presence of a sacrificial reductant **Red**, such as triethanolamine. Once the ring has received an electron, the interaction responsible for self-assembly is partly destroyed, and therefore the wire dethreads from the reduced ring. If oxygen is allowed to enter the solution, oxidation of the reduced bipyridinium unit restores the interaction and causes rethreading. The threading, dethreading, and rethreading

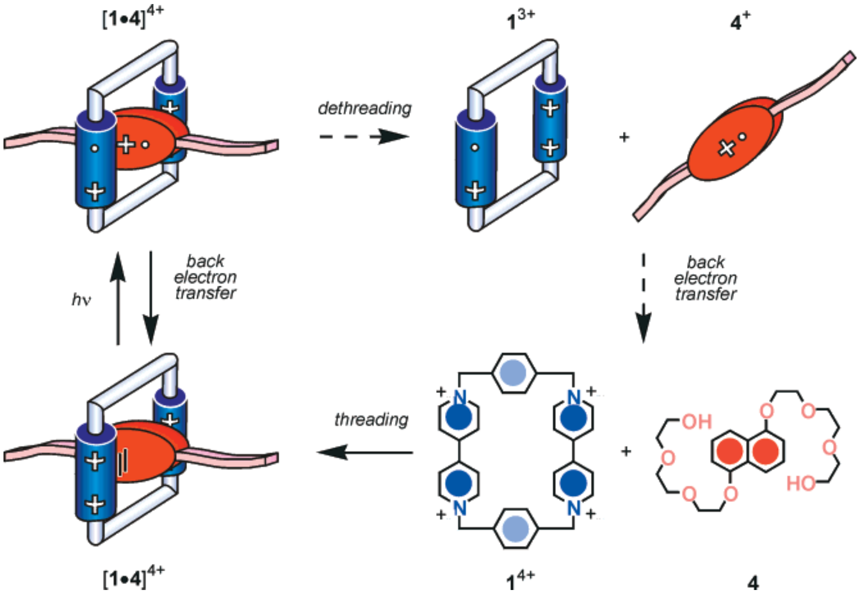

FIGURE 7. Light excitation of a pseudorotaxane based on CT interactions. The processes indicated by dashed arrows are unlikely to occur (see text).

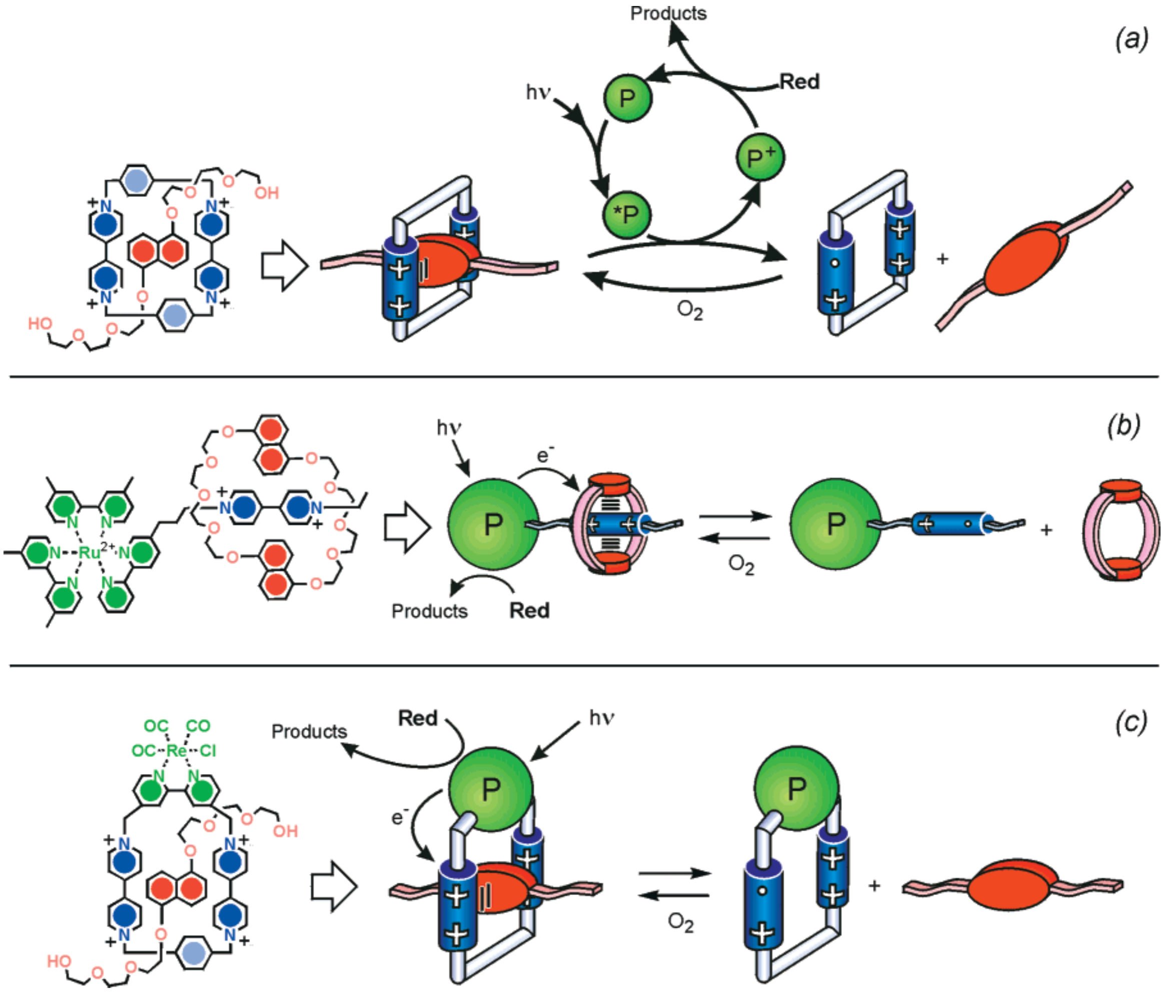

FIGURE 8. Light-driven dethreading of pseudorotaxanes by excitation of a photosensitizer **P** as (a) an external reactant (MeCN or H_2O, room temperature), (b) a stopper in the wire-type component (EtOH, room temperature), and (c) a component of the macrocyclic ring (H_2O, room temperature).

processes can be easily monitored by absorption and fluorescence spectroscopy.

Second generation photochemically driven piston/cylinder systems were then designed, in which the pseu-

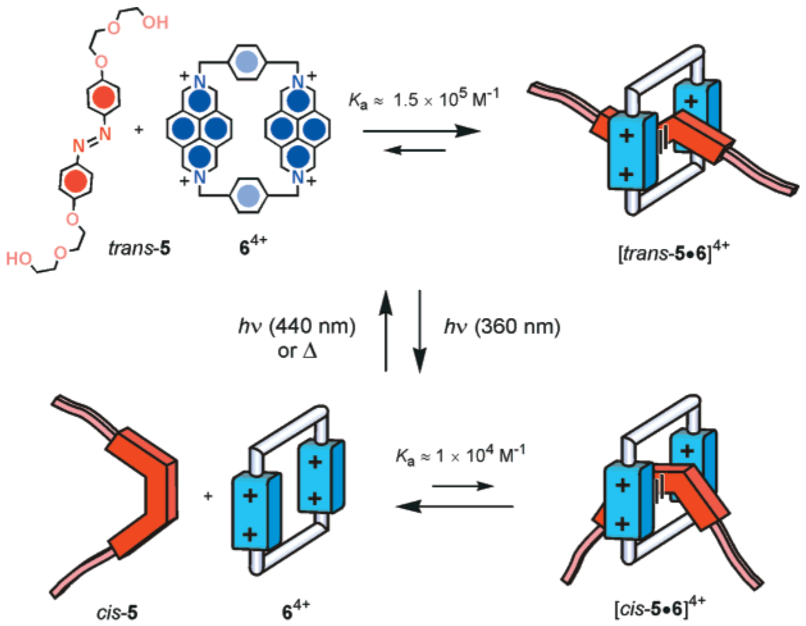

FIGURE 9. Controllable dethreading/rethreading of a pseudorotaxane based on a trans−cis photoisomerization reaction (MeCN, room temperature; 1×10^{-4} M *trans*-**5** and $\mathbf{6}^{4+}$, 80% complexed species).

dorotaxane structure incorporates the "light-fueled" motor (i.e., the photosensitizer) in the wire (Figure 8b)[19] or in the macrocyclic ring (Figure 8c).[20] In deaerated solution, excitation of the photosensitizer with visible light in the presence of a sacrificial donor causes, in both cases, reduction of the electron-acceptor unit, and, as a consequence, dethreading takes place. Rethreading can again be achieved by allowing oxygen to enter the solution. Many dethreading/rethreading cycles can be performed without any appreciable loss of signal until most of the reductant scavenger is consumed. It should be stressed, however, that photochemical systems which rely on such a sensitizer−scavenger strategy produce waste species.

A system in which dethreading/rethreading is exclusively governed by light energy, without generation of any waste product, is illustrated in Figure 9.[21] The threadlike species *trans*-**5,** which contains an azobiphenoxy electron-donor unit, and the electron-accepting host $\mathbf{6}^{4+}$ self-assemble very efficiently to give a pseudorotaxane. In the pseudorotaxane structure, the characteristic fluorescence of free $\mathbf{6}^{4+}$ is completely quenched by CT interactions. Irradiation with 360 nm light of a solution containing *trans*-**5** and $\mathbf{6}^{4+}$ causes photoisomerization of *trans*-**5** to *cis*-**5**. Since the cyclophane interaction with *cis*-**5** is much weaker than that with *trans*-**5**, photoexcitation causes a dethreading process, as indicated by the strong increase in the fluorescence intensity of $\mathbf{6}^{4+}$. On irradiation at 440 nm or by warming the solution in the dark, the trans isomer can be re-formed, and, as a result, it rethreads inside the cyclophane. Owing to the reversibility of the photoisomerization process, such a photochemical dethreading/rethreading cycle can be repeated at will.

7.2. A Photocontrollable Molecular Abacus. To achieve photoinduced ring switching in rotaxanes containing two different recognition sites in the dumbbell-shaped component, the cleverly designed compound $\mathbf{7}^{6+}$ shown in Figure 10 was synthesized.[22] This rotaxane is made of macrocycle **R** and a dumbbell component which contains (i) a photoactive Ru(II) polypyridine complex (**P**) as a stopper, (ii) a 4,4′-bipyridinium unit ($\mathbf{A_1}$) and a 3,3′-dimethyl-4,4′-bipyridinium unit ($\mathbf{A_2}$) as electron-accepting stations, (iii) a *p*-terphenyl-type ring system as a rigid spacer (**S**), and (iv) a tetraarylmethane group as the second stopper (**T**). The stable translational isomer is the one in which the **R** component encircles the better electron-acceptor $\mathbf{A_1}$ unit. To obtain the photoinduced abacus-like movement of macrocycle **R** between the $\mathbf{A_1}$ and $\mathbf{A_2}$ stations, two strategies have been devised. One is fully based on processes involving the rotaxane components (intramolecular mechanism), while the other one requires the help of external reactants (sacrificial mechanism). The latter strategy has been fully successful.[22]

The intramolecular mechanism, which implies the conversion of light energy into mechanical energy without generating waste products, is based on the four operations illustrated in Figure 10.

(a) Destabilization of the stable translational isomer: light excitation of **P** (step 1) is followed by the transfer of an electron to the $\mathbf{A_1}$ station (step 2), which is encircled by ring **R**; such a photoinduced electron-transfer process, which competes with the intrinsic excited-state decay (step 3), "deactivates" the $\mathbf{A_1}$ station.

(b) Ring displacement: the ring movement from $\mathbf{A_1}^-$ to $\mathbf{A_2}$ (step 4) has to compete with the back-electron-transfer process from $\mathbf{A_1}^-$ (still encircled by **R**) to the oxidized photoactive unit $\mathbf{P}^+$ (step 5).

(c) Electronic reset: the back-electron-transfer process from the "free" reduced station $\mathbf{A_1}^-$ to $\mathbf{P}^+$ (step 6) restores the electron-acceptor power to the $\mathbf{A_1}$ station.

(d) Nuclear reset: as a consequence of the electronic reset, back movement of the ring from $\mathbf{A_2}$ to $\mathbf{A_1}$ occurs (step 7).

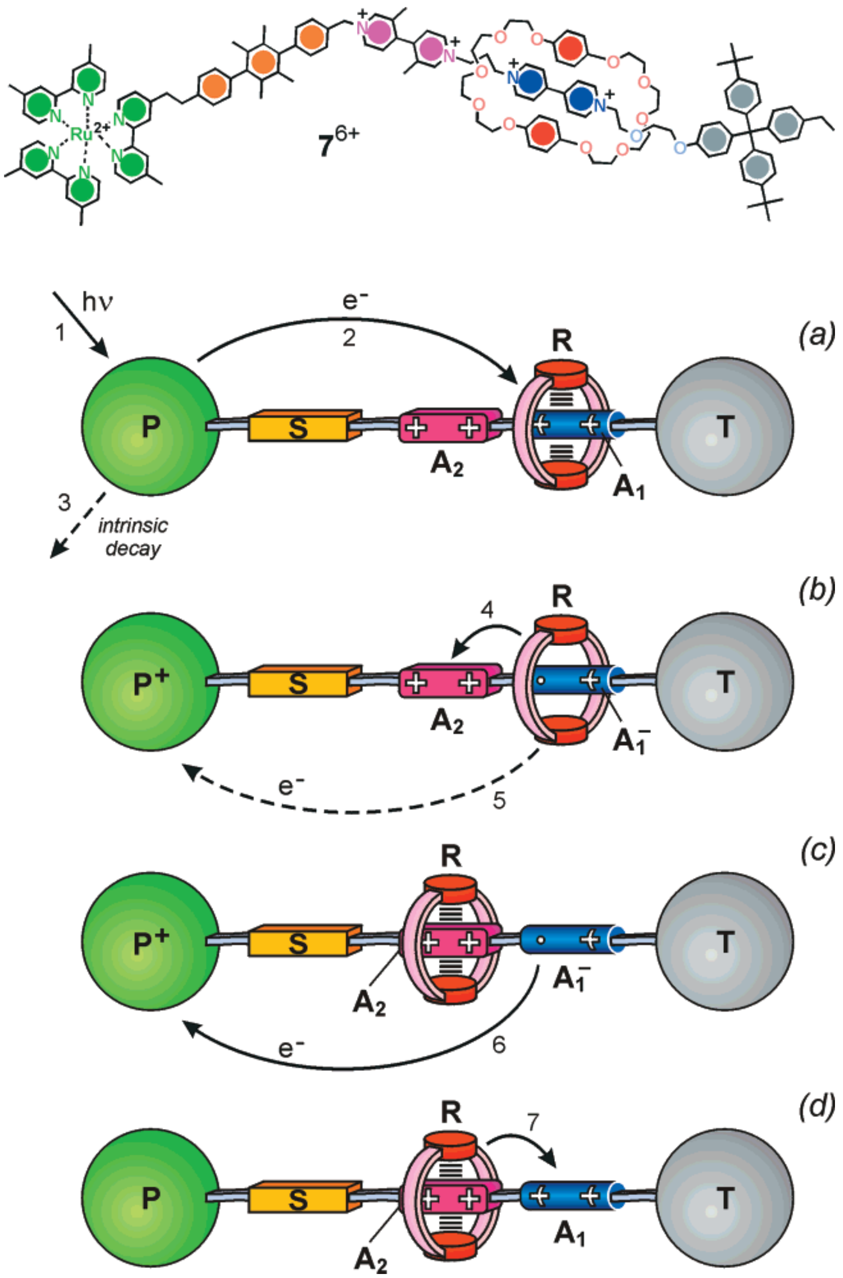

FIGURE 10. Rotaxane $\mathbf{7}^{6+}$ and schematic representation of the intramolecular mechanism for the photoinduced abacus-like movement of macrocycle **R** between the two stations $\mathbf{A_1}$ and $\mathbf{A_2}$.

The results obtained[22] seem to indicate that electronic reset of the system after light excitation (step 5) is faster than the ring displacement (step 4). Attempts to modify the system are currently in progress to further decrease the rate of the back-electron-transfer reaction (step 5) so as to achieve the displacement of the ring (step 4) before the occurrence of electronic reset.

It is worth noticing that in a system which behaves according to the intramolecular mechanism shown in Figure 10, each light input causes the occurrence of a forward and back ring movement (i.e., a full cycle) without generation of any waste product. In some way, it can be considered as a "four-stroke" cyclic linear motor powered by light.

8. Perspectives

The results so far achieved constitute the starting basis for the design of more sophisticated molecular-level machines. A few interesting possibilities are described below.

8.1. Three-Station Rotaxanes. It is possible to design rotaxanes in which the dumbbell component contains three different stations, e.g., a stronger ($\mathbf{A_1}$) and a weaker ($\mathbf{A_2}$) electron acceptor, and an appropriate amine/ammonium moiety. The $\mathbf{A_1}$ and $\mathbf{A_2}$ stations can be a 4,4′-bipyridinium and a 3,3′-dimethyl-4,4′-bipyridinium unit, respectively. Depending on the sequence in which the three stations are assembled, a suitable macrocyclic

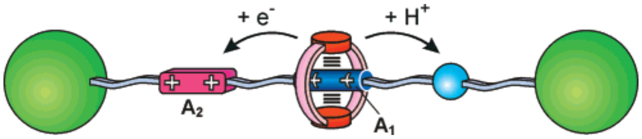

FIGURE 11. A three-station rotaxane in which the direction of ring displacement is determined by the selected input.

polyether component can be moved along the thread according to predetermined patterns. For example, with DB24C8 as a macrocycle and the three stations assembled as in Figure 11, the macrocycle which is originally located on the central station **A$_1$** can be displaced either toward the left-hand side by reduction of **A$_1$** or toward the right-hand site by protonation of the amine. By using the photoactive $[Ru(bpy)_3]^{2+}$ unit as a stopper, the reduction of **A$_1$** can be performed by light excitation.

The possibility to determine the direction along which the macrocycle can be moved by selecting the nature of the input opens the way to a variety of switching functions.

8.2. Rotaxanes as Carriers. The controlled movement of the ring component along the dumbbell in rotaxanes can be exploited to transport chemical species. Such a carrier function can be performed by appending to the shuttling macrocycle a host (or guest) unit capable of recognizing and linking an external species. In the example shown in Figure 12a, the dumbbell component of the rotaxane contains two different electron donors (e.g., a TTF and a DN unit), and the shuttling ring, which could be the previously seen cyclophane **1**$^{4+}$, is functionalized with a crown ether (e.g., [24]crown-8) capable of linking an ammonium species (e.g., anthracenylammonium). Shuttling of the cyclophane is controlled by electrochemical inputs, while loading and unloading of the transported amine can be controlled by acid/base inputs.

As a further elaboration of this concept, systems can be designed in which the transported species is driven to interact with another, appropriate unit. The system schematized in Figure 12b represents an example of redox-controlled formation of an exciplex via the rotaxane “rail”.

A number of other functions based on rotaxanes as carriers can be devised, such as stretching of a molecular spring (Figure 12c), a movement that could be at the basis of artificial molecular-level muscles.[23]

8.3. Unidirectional Ring Rotation in Catenanes. In catenanes such as that shown in Figure 5, it is possible to

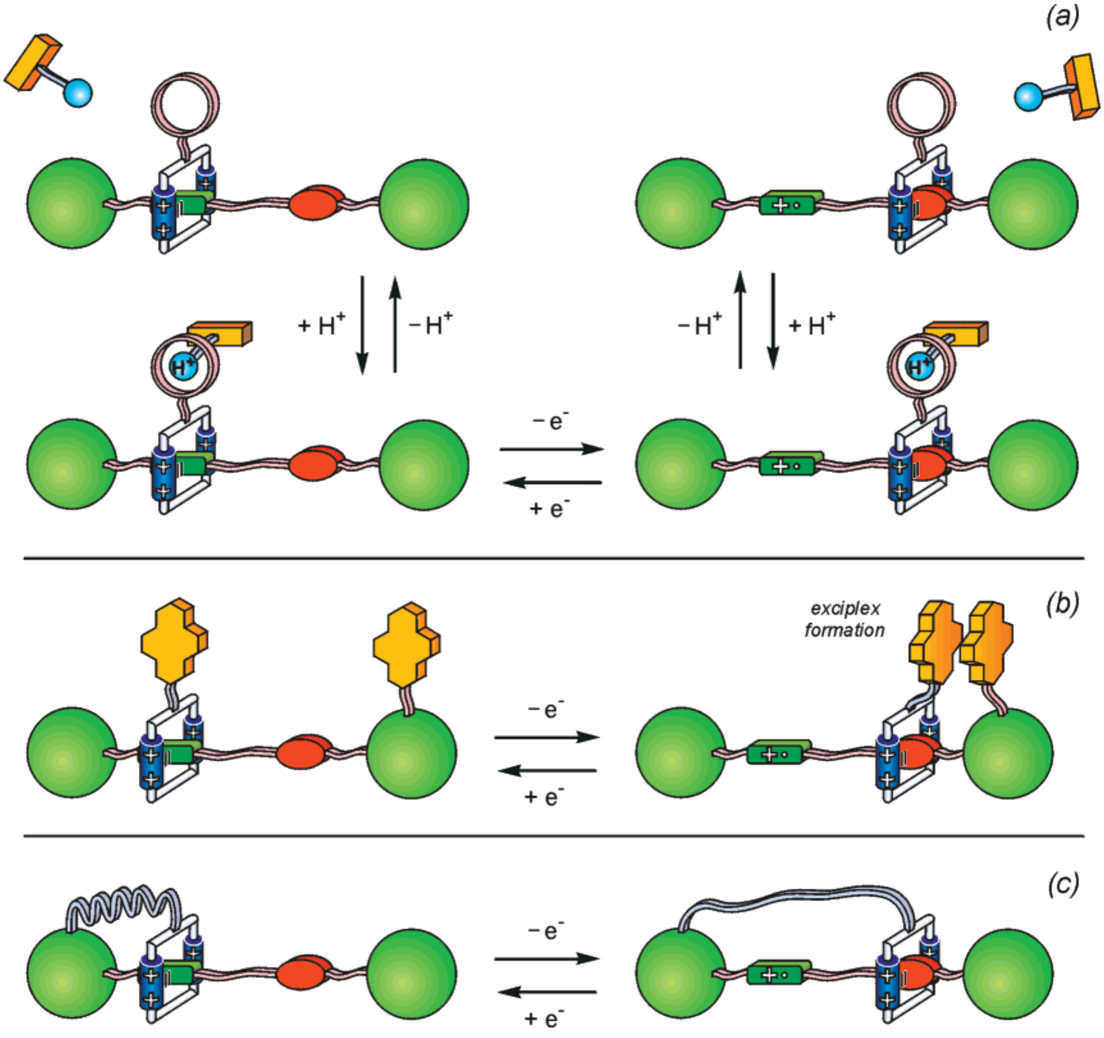

FIGURE 12. A rotaxane carrier powered by electrochemical inputs designed to perform (a) transport of an amine, (b) formation of an exciplex, and (c) stretching of a molecular spring.

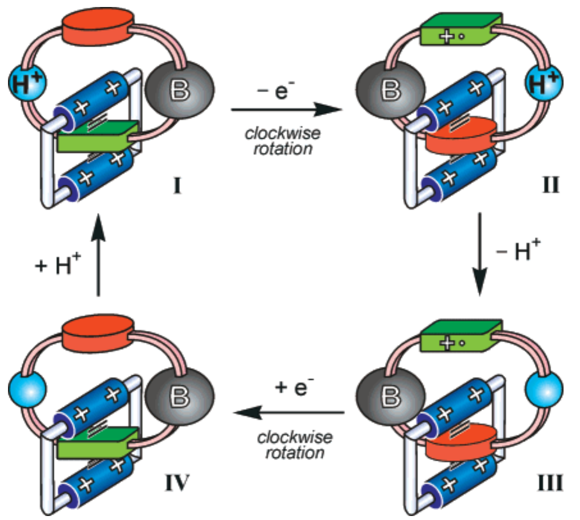

FIGURE 13. A catenane designed to perform as an electrochemically powered molecular-level rotary motor.

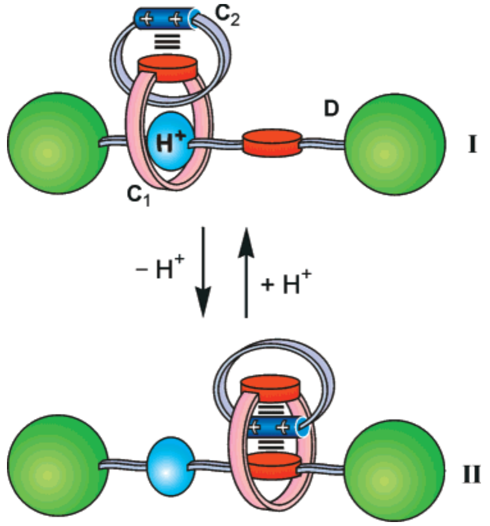

FIGURE 14. A rotacatenane designed to couple linear and rotary motions under acid/base stimuli.

cause a reversible switching between two different conformations, but there is no reason why this movement should happen via a unidirectional rotation of a ring around the other ring. To obtain a molecular-level rotary motor, the direction of each switching movement should be controllable. This goal can likely be reached with the catenane shown in Figure 13, which is derived from that displayed in Figure 5 by functionalizing the electron-donor macrocycle with an ammonium function and a bulky group **B**. In the starting conformation **I**, the better electron-donor TTF unit is inside the tetracationic cyclophane. When the TTF unit is oxidized, it has to escape from the cavity of the tetracationic cyclophane. The presence of the ammonium group favors clockwise rotation of the macrocycle over anticlockwise rotation, since the latter would imply threading of the 1+-charged ammonium unit through the 4+-charged cyclophane. The clockwise rotation leads to conformation **II,** in which the dioxynaphthalene unit is inside the cyclophane. At this stage, if deprotonation of the ammonium function is performed before reduction of the oxidized TTF unit (**III**), the preferred rotation, leading back TTF inside the cyclophane (**IV**), should again be clockwise because threading of the small amine unit into the cyclophane should compete favorably with that of the bulky group **B**. Protonation of **IV** regenerates **I**.

Such a catenane can be viewed as a four-stroke rotary motor working upon alternate redox and base/acid energy inputs. It is also worth noticing that, since all the processes are reversible, one can obtain anticlockwise rotation by inverting the order of the inputs.

8.4. Rotacatenane Molecular Gears. Combination of a catenane and a rotaxane in a supramolecular structure can lead to "second generation" molecular machines capable of coupling different mechanical movements. Examples of rotacatenanes are already available,[24] and by suitable design it should be possible to construct a molecular machine in which a "linear" shuttling motion is coupled with a "rotary" ring motion. In principle, this goal could be reached by the rotacatenane schematized in Figure 14, which is made of a macrocyclic crown ether $\mathbf{C_1}$ containing an electron-donor unit, interlocked with (i) a dumbbell component **D** containing an electron donor and a ammonium/amine function, and (ii) a macrocycle $\mathbf{C_2}$ containing an electron-acceptor unit. The working scheme of this machine should be as follows. In the rotacatenane protonated form **I**, the dumbbell component **D** occupies the cavity of macrocycle $\mathbf{C_1}$ with the ammonium function, while the acceptor unit of macrocycle $\mathbf{C_2}$ prefers an alongside interaction with the donor unit of $\mathbf{C_1}$ for steric and electrostatic reasons. Upon deprotonation, the amine function of **D** gets out of macrocycle $\mathbf{C_1}$ and the electron-acceptor moiety of $\mathbf{C_2}$ goes into $\mathbf{C_1}$ together with the electron-donor unit of **D** to give structure **II**, which is stabilized by donor–acceptor–donor stacking interactions. Reprotonation of the amine function of **D** reverses the movements and leads back to structure **I**.

More complex systems based on different energy inputs can also be conceived.

9. Conclusion

In the previously mentioned 1959 address to the American Physical Society, R. P. Feynman[2] concluded his reflection on the idea of constructing molecular-level machines as follows:

"What would be the utility of such machines? Who knows? I cannot see exactly what would happen, but I can hardly doubt that when we have some control of the rearrangement of things on a molecular scale we will get an enormously greater range of possible properties that substances can have, and of different things we can do."

Even though today rudimental molecular-level machines have been constructed and some of them have been proposed as possible components of chemical computers[25] and even exploited for the construction of practical devices,[14] we believe that Feynman's sentence is still the most appropriate final comment on the work described in this Account.

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References

(1) (a)Balzani, V.; Gómez-López, M.; Stoddart, J. F. Molecular Machines. *Acc. Chem. Res.* **1998**, *31*, 405−414. (b) Sauvage, J.-P. Transition Metal-Containing Rotaxanes and Catenanes in Motions: Toward Molecular Machines and Motors. *Acc. Chem. Res.* **1998**, *31*, 611−619. (c) Balzani, V.; Credi, A.; Venturi, M. Molecular-Level Devices. In *Supramolecular Science: Where It Is and Where It Is Going*; Ungaro, R., Dalcanale, E., Eds.; Kluwer: Dordrecht, 1999; pp 1−22. (d) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. Artificial Molecular Machines. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348−3391.

(2) Feynman, R. P. There's Plenty of Room at the Bottom. *Sat. Rev.* **1960**, *43*, 45−47.

(3) See, e.g.: Kelly, T. R.; De Silva, H.; Silva, R. A. Unidirectional Rotary Motion in a Molecular System. *Nature* **1999**, *401*, 150−152.

(4) Balzani, V.; Scandola, F. *Supramolecular Photochemistry*; Horwood: Chichester, 1991.

(5) Kaifer, A. E.; Gómez-Kaifer, M. *Supramolecular Electrochemistry*; Wiley-VCH: Weinheim, 1999.

(6) Koumura, N.; Zijlstra, R. W. J.; van Delden, R. A.; Harada, N.; Feringa, B. L. Light-driven Monodirectional Molecular Rotor. *Nature* **1999**, *401*, 152−155.

(7) Amabilino, D. B.; Stoddart, J. F. Interlocked and Interwined Structures and Superstructures. *Chem. Rev.* **1995**, *95*, 2725−2828.

(8) Credi, A.; Balzani, V.; Langford, S. J.; Stoddart, J. F. Logic Operations at the Molecular Level. An XOR Gate Based on a Molecular Machine. *J. Am. Chem. Soc.* **1997**, *119*, 2679−2681.

(9) Ishow, E.; Credi, A.; Balzani, V.; Spadola, F.; Mandolini, L. A Molecular-level Plug/socket System. *Chem. Eur. J.* **1999**, *5*, 984−989.

(10) Ballardini, R.; Balzani, V.; Clemente-Leon, M.; Credi, A.; Gandolfi, M. T.; Ishow, E.; Martinez-Diaz, M.-V.; Stoddart, J. F.; Wenger, S. Manuscript in preparation.

(11) Ashton, P. R.; Ballardini, R.; Balzani, V.; Baxter, I.; Credi, A.; Fyfe, M. C. T.; Gandolfi, M. T.; Gómez-López, M.; Martínez-Díaz, M. V.; Piersanti, A.; Spencer, N.; Stoddart, J. F.; Venturi, M.; White, A. J. P.; Williams, D. J. Acid−base Controllable Molecular Shuttles. *J. Am. Chem. Soc.* **1998**, *120*, 11932−11942.

(12) Molecular Logic Arrives. *Sci. Comput. World* **1999**, February/March, 11.

(13) Asakawa, M.; Ashton, P. R.; Balzani, V.; Credi, A.; Hamers, C.; Mattersteig, G.; Montalti, M.; Shipway, A. N.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. A Chemically and Electrochemically Switchable [2]Catenane Incorporating a Tetrathiafulvalene Unit. *Angew. Chem., Int. Ed.* **1998**, *37*, 333−337.

(14) Collier, C. P.; Mattersteig, G.; Wong, E. W.; Beverly, K.; Sampaio, J.; Raymo, F. M.; Stoddart, J. F.; Heath, J. R. A [2]catenane-based Solid State Electronically Reconfigurable Switch. *Science* **2000**, *289*, 1172−1175.

(15) Ashton, P. R.; Baldoni, V.; Balzani, V.; Credi, A.; Hoffmann, H. D. A.; Martinez-Diaz, M.-V.; Raymo, F. M.; Stoddart, J. F.; Venturi, M. Dual Mode Co-conformational Switching in Catenanes Incorporating Bipyridinium and Dialkylammonium Recognition Sites. *Chem. Eur. J.*, in press.

(16) This result is apparently in contradiction with the fact that in the rotaxane discussed in section 5.2, the more stable isomer is the one in which the macrocycle surrounds the ammonium center. Clearly, both the CT and hydrogen-bonding interactions are affected by the number, dimension, and spatial arrangement of the interacting units.

(17) Ballardini, R.; Balzani, V.; Gandolfi, M. T.; Prodi, L.; Venturi, M.; Philp, D.; Ricketts, H. G.; Stoddart, J. F. A Photochemically-driven Molecular Machine. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1301−1303.

(18) Benniston, A. C.; Harriman, A.; Yufit, D. S. Artificial Phototropism: Reversible Photoseparation of Self-assembled Interlocking Conjugates. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2356−2358.

(19) Ashton, P. R.; Ballardini, R.; Balzani, V.; Constable, E. C.; Credi, A.; Kocian, O.; Langford, S. J.; Preece, J. A.; Prodi, L.; Schofield, E. R.; Spencer, N.; Stoddart, J. F.; Wenger, S. Ru(II)-polypyridine Complexes Covalently Linked to Electron Acceptors as Wires for Light-driven Pseudorotaxane-type Molecular Machines. *Chem. Eur. J.* **1998**, *4*, 2411−2422.

(20) Ashton, P. R.; Balzani, V.; Kocian, O.; Prodi, L.; Spencer, N.; Stoddart, J. F. A Light-fueled "Piston-cylinder" Molecular-level Machine. *J. Am. Chem. Soc.* **1998**, *120*, 11190−11191.

(21) (a)Asakawa, M.; Ashton, P. R.; Balzani, V.; Brown, C. L.; Credi, A.; Matthews, O. A.; Newton, S. P.; Raymo, F. M.; Shipway, A. N.; Spencer, N.; Quick, A.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. Photoactive Azobenzene-containing Supramolecular Complexes and Related Interlocked Molecular Compounds. *Chem. Eur. J.* **1999**, *5*, 860−875. (b) Balzani, V.; Credi, A.; Marchioni, F.; Stoddart, J. F. Artificial Molecular-level Machines. Dethreading/rethreading of a Pseudorotaxane Powered Exclusively by Light Energy. Submitted.

(22) Ashton, P. R.; Ballardini, R.; Balzani, V.; Credi, A.; Dress, K. R., Ishow, E.; Kleverlaan, C. J.; Kocian, O.; Preece, J. A.; Spencer, N.; Stoddart, J. F.; Venturi, M.; Wenger, S. A Photochemically Driven Molecular-level Abacus. *Chem. Eur. J.* **2000**, *6*, 3558−3574.

(23) A first example of artificial molecular-level muscles has been recently reported: Jimenez, M. C.; Dietrich-Buchecker, C.; Sauvage, J.-P. Towards Synthetic Molecular Muscles: Contraction and Stretching of a Linear Rotaxane Dimer. *Angew. Chem., Int. Ed.* **2000**, *39*, 3284−3287.

(24) Amabilino, D. B.; Ashton, P. R.; Bravo, J. A.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. Template-directed Synthesis of a Rotacatenane. *Eur. J. Org. Chem.* **1999**, 1295−1302.

(25) Ball, P. Chemistry Meets Computing. *Nature* **2000**, *406*, 118−120.

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