Molecular Machines

Chemistry in Motion—Unidirectional Rotating Molecular Motors

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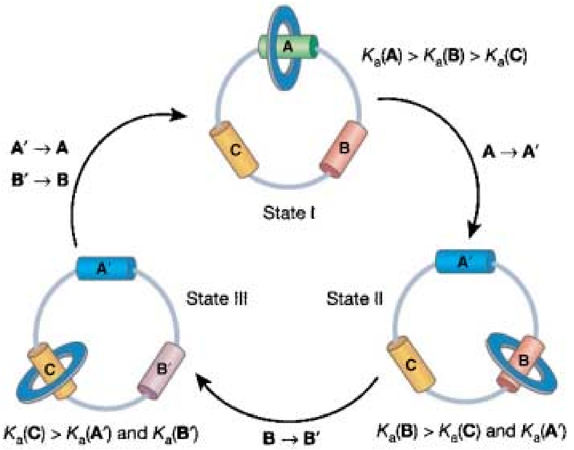
Keywords:
catenanes · isomerization · macrocycles · photochemistry

Molecules are in constant motion, if not frozen around 0 K, but their Brownian motion is random. Overcoming this randomizing effect and generating directional motion at the molecular level with artificial systems is still a challenge. Research in this area is inspired by the vision of transferring the concept of an engine or a motor to the molecular level.[1] That this is possible is illustrated by the directional processes found in nature:[2] cell division, translocation of organelles, and membrane transport all rely on directional movement, while processes such as replication, transcription, and translation require encoded information sequences to be read and copied in a directional manner.

Macroscopic engines and molecular motors both convert chemical, electrical, or light energy into mechanical work, yet their mode of operation is very different.[3] Because of their dimensions molecular motors must operate at energies only slightly higher than those of the thermal bath surrounding them.[4] They are actuated by Brownian motion and the key to their function is to give a direction to these undirected processes. Chemistry's role is to select one direction from all possible movements by lowering the energy profile of this directional movement compared to all the others. This makes this movement happen preferentially.[5] Chemical or photochemical steps fuel these selection processes.

Leigh et al.[6] recently reported a net relative unidirectional circumrotation in a mechanically interlocked molecular rotor.[7] The [2]catenane system (Scheme 1) consists of a larger macrocycle which contains three stations with different binding affinities[8] for the smaller macrocycle [$K_a(\mathrm{A}) > K_a(\mathrm{B}) > K_a(\mathrm{C})$]. The stimuli-induced sequential movement of the smaller ring along the larger one goes through three photochemical and thermal steps, which alter the binding affinities of the stations. As a result the small ring is switched between the three different stations with positional integrity from A to B to C to A. However, the rotation in this system is not unidirectional because the small ring can move from A to B directly or via station C.



Scheme 1. Bidirectional sequential movement between three different binding sites in a [2]catenane.

A four-station [3]catenane overcomes this problem (Scheme 2). Initially the blue and purple small rings are bound to stations A and B, respectively. With long wavelength UV light irradiation (process 1) A is converted into A′ with lower binding affinity for the small blue ring, which becomes free to move. The purple ring stays at the B station blocking any clockwise movement of the blue ring, which has to move counterclockwise to arrive at station C, which now has the highest binding affinity. Irradiation with short wavelength UV light (process 2) transforms B into B′ breaking the hydrogen bonds that hold the purple ring. The purple ring moves counterclockwise to station D, where it is bound again. The clockwise direction is blocked by the blue ring. White light irradiation (process 3) then resets the system by switching A′ back to A and B′ back to B, which makes the blue ring move to B and the purple ring move to A in a unidirectional manner. The blue and the purple ring have exchanged places by following each other halfway around the large macrocycle. To complete a full rotation steps 1 to 3 have to be repeated. Each ring has then performed one clockwise and three counterclockwise movements, which amounts to a net relative unidirectional motion.[9]

Each step puts the system in a nonequilibrium state, from where it relaxes by Brownian motion into the new global minimum. To make the process directional, the kinetics of the

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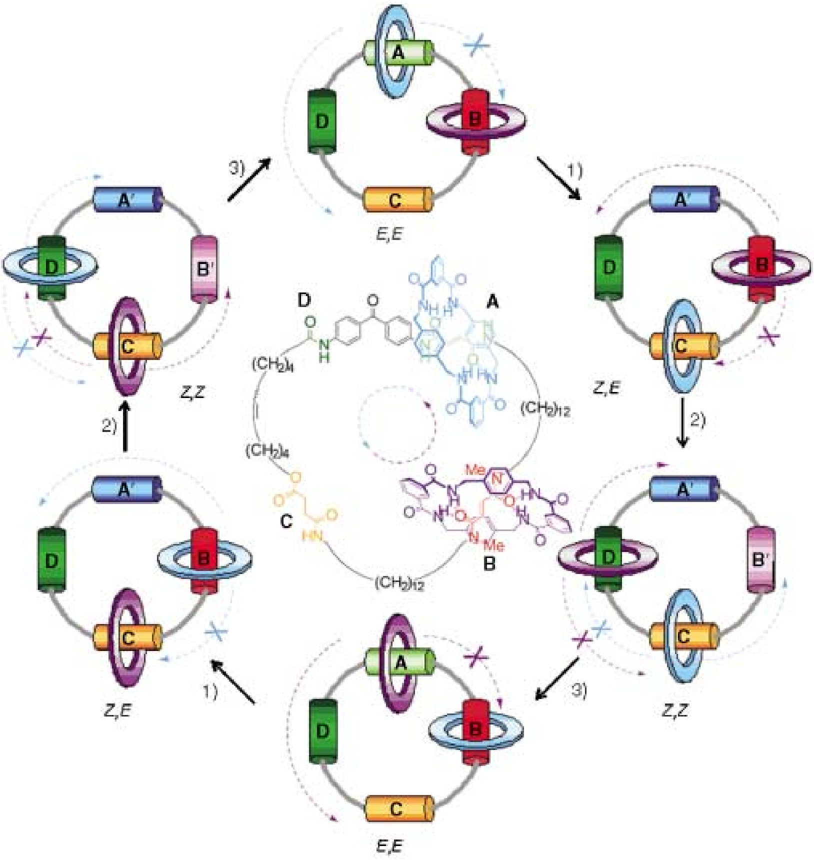
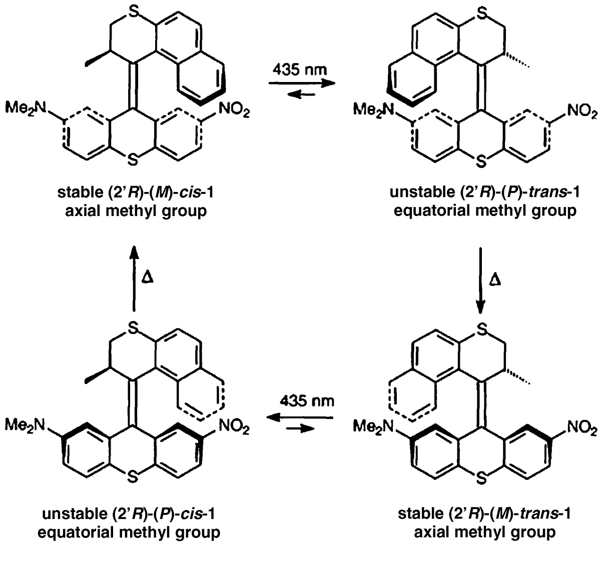
DOI: 10.1002/anie.200301697



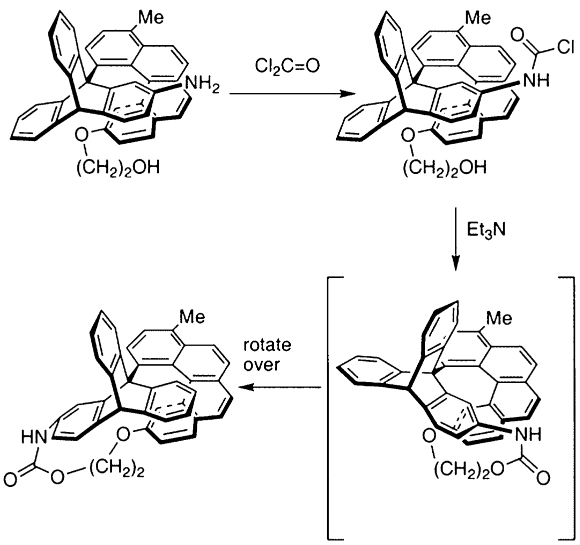
Scheme 2. Stimuli-induced net unidirectional circumrotation in a four-station [3]catenane. The overall process corresponds to a relative counterclockwise movement. See text for an explanation of the individual steps.

different routes for reaching thermodynamic equilibrium must be controlled so as to favor only one. Two previously reported unidirectional rotating molecular motors, although structurally very different, use the same principle. The Feringa system[10,11] is based on a chiral helical alkene, which displays unidirectional rotation around the central C–C double bond in four isomerization steps induced by UV light and temperature changes.[12] The chirality of the system is needed to create the unidirectional motion and, in addition, enables monitoring of the process by CD spectroscopy. A second generation of Feringa's molecular motors (Scheme 3) has meanwhile been developed,[13,14] allowing faster and even continuous rotation as well as the use of visible light.[15] Remarkably, the presence of a single stereogenic center in these systems is sufficient to ensure unidirectional rotation. The inclusion of the molecular motors in a cholesteric liquid crystalline film makes it possible to switch the film color through irradiation,[16] leading to observable macroscopic effects induced by the dopant.[17]

The Kelly motor[18–20] rotates around a triptycene/helicene bond and is chemically fueled[21] by phosgene. Three subsequent reaction and hydrolysis steps are needed to complete one third of a turn (Scheme 4).[22] As published so far, the system is incapable of undergoing a full rotation. The direction of motion in the molecular motors reported by Kelly and co-workers and Feringa and co-workers is determined by the configuration of the substance. The catenanes described by Leigh et al. are not chiral, which shows that chirality is not a prerequisite for net relative directional work with a rotating machine at the molecular level.



Scheme 3. Unidirectionally rotating molecular motor developed by Feringa et al. which is driven by visible light.



Scheme 4. One-third rotation of Kelly's chemically fueled motor.

Having achieved unidirectional motion with molecular motors, the questions immediately arise as to what work they can do and what they can drive. The transformation of circumrotation into mechanical work is difficult. To achieve macroscopic forces and effects, ordered immobilization and coordination of action seems necessary, independent of the type of molecular motor. In this regard artificial systems that show stimulated linear motion[23] based on polymers with molecular recognition sites, as recently reported by Schneider et al.,[24] may be easier to use. We will surely see more examples of receptor-based molecular machines[25] with increasing performance in the future, but it is still a long way to their practical application.

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[3] C. Bustamante, D. Keller, G. Oster, *Acc. Chem. Res.* **2001**, *34*, 412 – 420.

[4] Excess energy is quickly dissipated into the surrounding environment.

[5] This is true for the "Brownian ratchet" model, which most systems published so far are based on. Alternatively, the "power stroke" model is triggered by a conformational change induced by bonding or reaction of an energy-rich molecule, which results in movement of the motor.

[6] D. A. Leigh, J. K. Y. Wong, F. Dehez, F. Zerbetto, *Nature* **2003**, *424*, 174 – 179.

[7] For a review of rotaxane-based molecular motors, see: C. A. Schalley, K. Beizah, F. Vögtle, *Acc. Chem. Res.* **2001**, *34*, 465 – 476.

[8] Determined by the individual association constants K_a.

[9] The direction of rotation in a three-dimensional world is always relative to a reference point. For instance, the turning of a spinning wheel appears to be clockwise or counterclockwise depending on whether the observer is in front or behind the wheel, even though the movement of the wheel is identical for both cases.

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[23] Transition-metal-based linear molecular machines: a) M. C. Jimenez-Molero, C. Dietrich-Buchecker, J. P. Sauvage, *Chem. Commun.* **2003**, 1613 – 1616; b) J. P. Collin, C. Dietrich-Buchecker, P. Gavina, M. C. Jimenez-Molero, J. P. Sauvage, *Acc. Chem. Res.* **2001**, *34*, 477 – 487; c) an entropy-driven bistable system has been described recently by Leigh et al.: G. Bottari, F. Dehez, D. A. Leigh, P. J. Nash, E. M. Pérez, J. K. Y. Wong, F. Zerbetto, *Angew. Chem.* **2003**, *115*, 6066 – 6069; *Angew. Chem. Int. Ed.* **2003**, *42*, 5886 – 5889.

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