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Light-driven molecular switches and motors

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ABSTRACT Technology is omnipresent in our modern-day society and it is hard to imagine a world without machines, computers or robots. One of the main current scientific challenges is the bottom-up construction of systems that represent nanosize analogues of switches, devices and motors. Our efforts in this area have focussed on the construction of devices based on sterically overcrowded alkenes. In this paper, we present our ongoing research on the construction of binary molecular switches, which has recently led to genuine molecular motors. The control of chirality in a molecular switching system allows interconversion between molecules of opposite helicity using different wavelengths of light. Such bistable chiral switches are of potential use in optical data storage and processing at the molecular level. The control of molecular chirality is even more subtle in the case of molecular motor systems. The exquisite control of chirality using light as an energy source has resulted in a controlled, repetitive 360° unidirectional rotation in two generations of molecular motor systems.

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1 Introduction

It is hard to imagine daily life without motors [1]. Controlled rotary and linear motion is at the heart of the variety of machinery our society depends on. For most individuals it goes unnoticed that at any instant numerous molecular motors are also engaged in our body to control such delicate processes as catalysis, transport and muscle movement. The fascinating molecular motors discovered in biological systems such as the ATP-ase rotary and muscle linear motors [2]

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offer a great source of inspiration to design synthetic motor systems in which controlled translational or rotary motion can be accomplished [3]. It is evident that the development of macroscopic engines was decisive during the industrial revolution and it is tempting to ascribe a similar role for molecular motors in the development of nanotechnology ahead of us [4].

The bottom-up construction of molecular motors, in which chemical energy is converted into mechanical energy leading to controlled motion, offers a formidable challenge. In designing molecular motors one has to take into consideration that, compared to ordinary motors, where energy input induces motion, in molecular motors energy input also has to restrain motion [3]. Rotary motion around a single carbon-carbon bond in an alkane for instance is extremely fast with an energy barrier of only 20 kJ mol⁻¹ (rate 2×10^9 s⁻¹ at 25 °C) and there is no control over the directionality of the rotary motion [5]. Illustrative for simple thermal movement are also rotary and linear motions in biaryls and rotaxanes, respectively (Fig. 1).

The problem of mutual random thermal motion of molecules has recently been emphasized in discussions on ratchet-type molecular motors (“if you can’t beat the chaos why not exploit it”) [3b] and nanomachines (“navigators on the nanoscale have to accommodate to the Brownian storms”) [6]. In synthetic approaches towards artificial machinery a variety of molecular and supramolecular systems have been designed in which an external chemical, electrochemical or photochemical stimulus induces a switching process or movement within the molecule or triggers a change in shape or assembly of molecules [7]. These systems include molecular propellers [7a, 8a], brakes [8b], switches [7c], turnstiles [8c], ratchets [3b, 8d, 8e], shuttles [7b, 7d, 7e] and muscles [8f]. We envisioned that three basic prerequisites need to be ful-

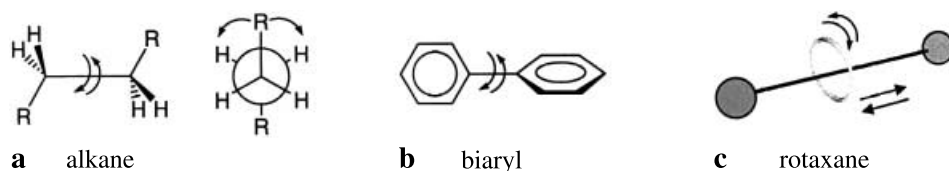
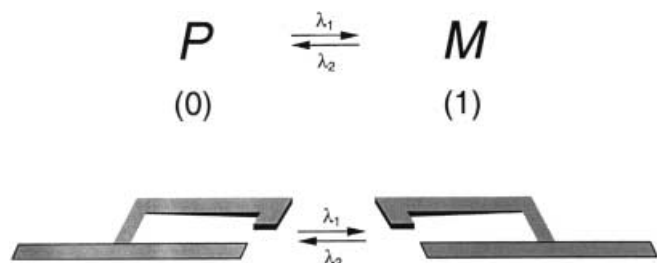


FIGURE 1 Thermal rotary and linear motions in **a** alkane, **b** biaryl, and **c** rotaxane

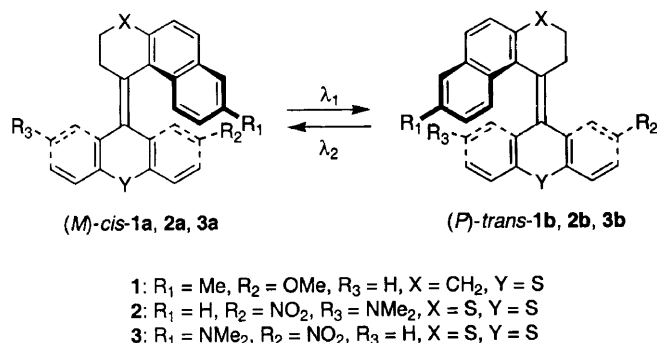
filled, however, in order to be able to construct a molecular motor: (i) repetitive 360° rotary motion; (ii) consumption of energy and (iii) unidirectional rotation. Until the recent report on the first rotary motor [9, 10] none of the synthetic systems could be classified as a motor according to these requirements. The research discussed here was inspired by the process of vision in which a light-induced *cis*–*trans* isomerization of an alkene moiety in retinal induces a motion in the molecule, changing it from a bend to a linear shape [7c, 11]. The exploitation of similar photoisomerization processes in chiral, helical-shaped, alkenes allowed the construction of chiral optical (chiroptical) molecular switches and the first light-driven molecular motor which undergoes repetitive 360° rotations in a unidirectional manner. The principles of chiroptical molecular switches and light-induced unidirectional rotary motion, the application as trigger elements and multifunctional molecular switches as well as the first- and second-generation light-driven molecular motors will be discussed.

1.1 Chiroptical molecular switches

The principle of the chiroptical switch is illustrated in Scheme 1. The molecular design is based on a lower half, considered the static part, and an upper half connected by a central carbon–carbon double bond, this being the axis. Upon irradiation the upper part turns from right to left with a simultaneous change in helicity of the molecule. The left- (*M*) and right- (*P*) handed forms of such a chiral molecule, which can be interconverted by light, represent two distinct states in a binary logic element [7c, 12].



The molecular structures comprise unsymmetric sterically overcrowded alkenes 1–3.



In order to avoid unfavorable steric interactions at the 'fjord region' these molecules adopt a helical shape; either a left-handed (*M*)-helix or a right-handed (*P*)-helix is present.

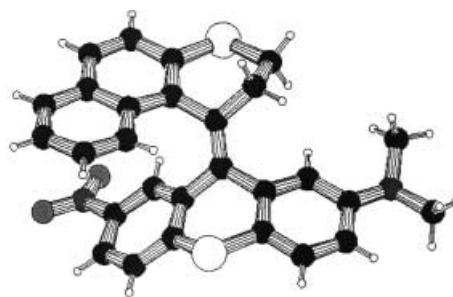


FIGURE 2 Molecular structure of (*P*)-*cis*-2a

The molecular structure of (*P*)-*cis*-2a (Fig. 2) is illustrative for the antifolded helical shape of these chiral alkenes.

The central double bond (the axis) has a normal bond length (1.353 Å) and shows only a slight deviation from planarity. Due to the presence of substituents in these compounds *cis*-1–3 and *trans*-1–3 are pseudoenantiomers; the overall helicity of the *cis* and *trans* forms is roughly mirror image. The assignment of structures of *cis*- and *trans*-isomers was based on NMR studies. Switching between the photobistable *M* and *P* forms can be accomplished at two different wavelengths λ_1 and λ_2 . In the first successful chiroptical molecular switch 1, indeed a stereospecific interconversion between (*M*)-*cis*-1a and (*P*)-*trans*-1b could be accomplished using 259-nm and 300-nm light, respectively [13]. The modest 4% shift in photostationary states was accompanied by approximately 10% racemization after 20 switching cycles. The introduction of a naphtho[2,1-*b*]thiopyran upper half and nitro-acceptor and dimethylamine-donor moieties in the lower half, as in 2, results in remarkably enhanced stability and reversibility and a bathochromic shift in the absorption spectra. This allows switching near the visible, leading to photostationary states with large differences in helicity [14]. Using 365-nm light a (*M*)-2a/(*P*)-2b ratio of 30 : 70 and with 435-nm light a 90 : 10 ratio of (*M*)-2a/(*P*)-2b was observed, respectively. The photomodulation of chirality, as de-

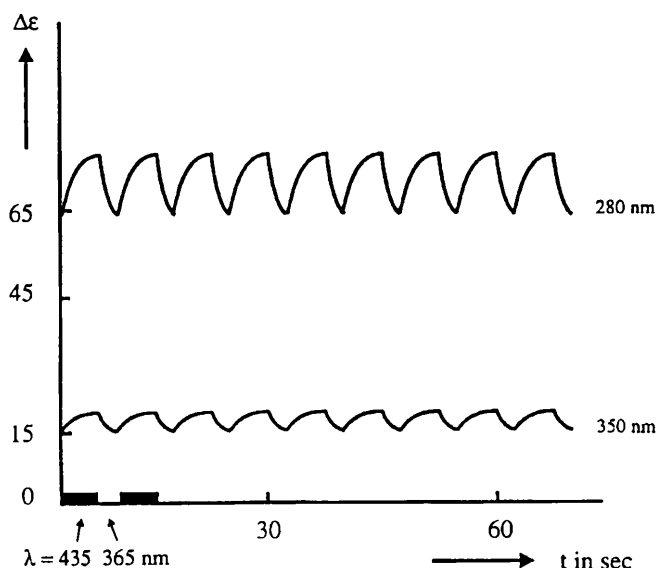


FIGURE 3 Photoswitching of (*M*)-*cis*-2a and (*P*)-*trans*-2b as detected by CD spectroscopy

tected by circular dichroism (CD) spectroscopy, is shown in Fig. 3.

It is important to note that **2a** is perfectly stable towards thermal racemization (helix inversion of (*M*)-*cis*-**2a** to (*P*)-*cis*-**2a**) under ambient conditions ($\Delta G_{\text{rac}} = 122.2 \text{ kJ mol}^{-1}$). Due to the light-induced motion around the central alkene bond the naphthalene moiety in the upper part can be positioned either facing the electron-acceptor group (in (*M*)-*cis*-**2a**) or facing the electron-donor group (in (*P*)-*trans*-**2b**) in the lower half. The difference in electron donor–acceptor interaction could be further enhanced in compound **3** with a dimethylamine donor group in the upper half. Irradiation at 435 nm resulted in a highly stereoselective switching process in one direction, leading to a (*M*)-*cis*-**3**/*(P)*-*trans*-**3** ratio of 99 : 1. Unfortunately, reversibility in this case was only modest [15]. These light-induced switching processes represent very clean, energy-consuming, molecular motions with the benefit that the properties of these molecules can be readily tuned through modifications in substituents and structures. Using similar helical-shaped photobistable alkenes, switching between enantiomers at a single wavelength of light could also be accomplished and, although the slight stereochemical bias that was found is not particularly useful for control of motion, it can be amplified in a liquid-crystal (LC) film [16].

A major advantage of these chiral optical switches, compared to other photochromic compounds used as molecular memory or data-storage elements, is the possibility of nondestructive read-out of an optical recording system containing these materials. The change in optical rotation can simply be monitored at wavelengths remote from the wavelengths used for switching [12]. In the context of the discussion on controlled motion at the molecular level, it should be emphasized that the relative direction of the movement in these systems can be controlled by the wavelength of the light and depends only on the helicity of the molecule. These chiroptical switches represent the first example of a synthetic system in which unidirectional rotary motion is achieved.

1.2 Control of organization by chiroptical molecular switches

A particularly appealing application of molecular switches is their use as trigger elements to control properties of materials in a reversible manner. Liquid-crystalline materials are attractive candidates as the molecular orientation and mesophases are known to be often highly sensitive to the nature of dopant molecules present in the LC phase [17]. The light-induced motion and change in helicity in the chiroptical switches might be capable of controlling the organization in the large ensemble of mesoscopic molecules. Photoswitching of LC phases by light via chiral photochromic guest molecules offers an alternative to current methods of addressing display materials [18]. When (*P*)-*trans*-**2b** or (*M*)-*cis*-**2a** were employed as chiral dopant (1 wt %) in nematic 4'-(pentyl)-4-biphenylcarbonitrile **4**, cholesteric phases of opposite handedness were obtained. Furthermore, due to different switching efficiencies, when an excess of (*M*)-*cis*-**2a** is present a distinctly larger pitch of the cholesteric phase is observed than in

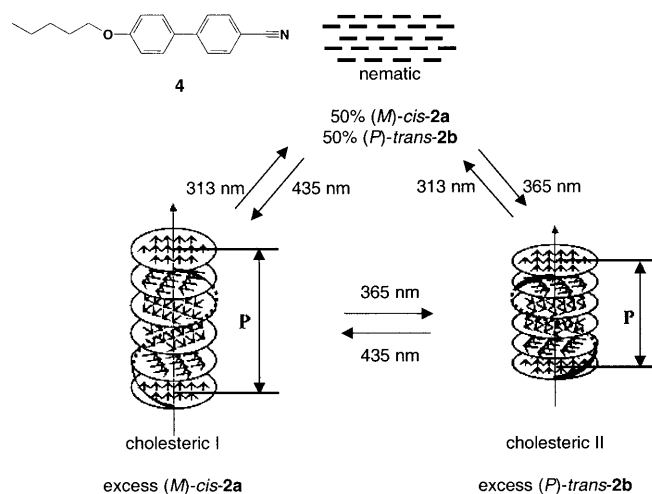


FIGURE 4 Photochemical modulation of doped liquid crystalline phases

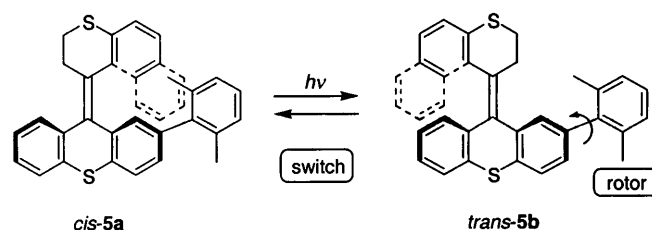
the situation with an excess of (*P*)-*trans*-**2b** present as dopant (Fig. 4).

Alternated irradiation at 435 nm and 365 nm results in photomodulation of the pitch between values of $12.29 \mu\text{m}$ and $5.31 \mu\text{m}$ as well as simultaneous reversal of the helical screw sense. Irradiation at 313 nm turned the cholesteric phase into a nematic phase. In fact a compensated nematic phase is formed due to the formation of a near 50 : 50 ratio of opposite helices (pseudoracemate) of the photoactive guest molecule. Subsequent irradiation at either 435 nm or 365 nm switched the chirality of the mesophase on again.

The motion and simultaneous change in helicity induced in the photoactive molecule is therefore amplified in the motion and reorganization of a large ensemble of molecules in the LC phase. The LC switch shown in Fig. 4 comprises a three-stage system with full reversibility [19], but it should be noted that all states in between two extreme cholesteric phases can be addressed, resulting in a multistate LC switch.

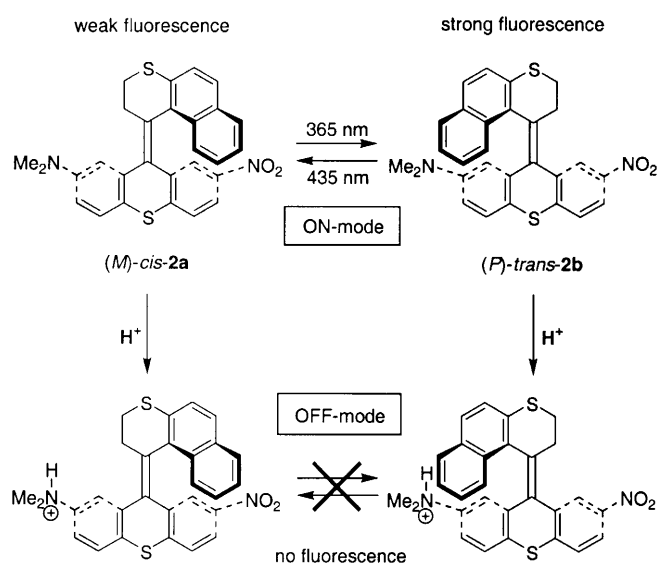
1.3 Molecular brakes

These systems were designed to control the speed of rotation or to block the rotary motion via an additional function (besides the switch function) present in the molecules. The switchable molecular rotor shown here was constructed in order to control the speed of rotation or even blocking the rotation around a carbon–carbon single bond [8a]. A thioxanthene-based switch and a biaryl rotor are present in the same molecule. Photoisomerization of *cis*-**5a** to *trans*-**5b** would move the upper naphthalene moiety away from the rotor, resulting in a distinct decrease in steric hindrance for biaryl rotation and as a consequence a faster propeller motion.



Surprisingly, barriers for biaryl rotation of $\Delta G^\ddagger = 79.5$ and 82.4 kJ mol^{-1} were observed by temperature-dependent NMR studies for *cis*-**5a** and *trans*-**5b**, respectively. Model studies and semiempirical calculations on the structures and dynamic processes confirmed the higher barrier for the *trans*-isomer. In the *cis*-isomer-**5a** the naphthalene upper part easily bends away to allow passage of the rotor, whereas in the case of *trans*-**5b** the methyl substituents of the rotor interfere with the methylene groups of the upper part. These studies provide the guiding principles for precise control of the propeller type of rotary motion.

In contrast to the steric control of the rotary motion discussed above, the system shown below comprises chemical control of a light-induced motion [20]. The photochemical switching process of the donor–acceptor-substituted helical alkene **2** could be blocked completely by protonation of the N,N-dimethylamine donor moiety.



In this system both the presence of a donor- and an acceptor-substituent are essential for photoisomerization. Protonation with trifluoroacetic acid of the amine group results in an acceptor–acceptor (ammonium and nitro)-substituted lower half and as a result the photochemical switching is blocked. Deprotonation restores the donor amine group and therefore the switching is on again. The reversible protonation constitutes a brake effect, as by simple (de)protonation the on mode (switching) and off mode (no switching) are addressed. Three distinct states can be readily detected as the fluorescence emission is also modulated by light and (de)protonation in this system (Scheme 4).

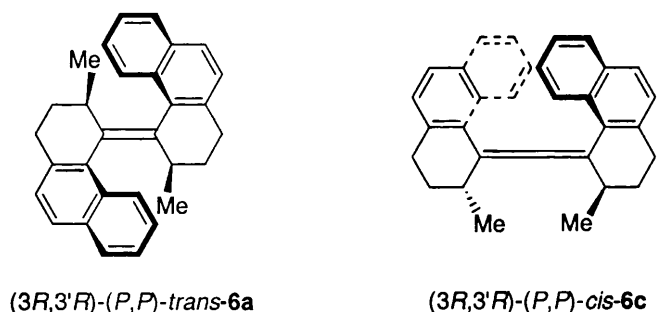
1.4 First-generation light-driven motors

Although a distinct and unidirectional rotary motion around a central bond was induced in the molecular switches discussed above, these systems are far from motors in view of the prerequisites formulated earlier. In order to act as a motor the means have to be found to continue the light-induced motion upon switching in the same direction to complete a 360° cycle. The construction of chiral overcrowded

alkene (3*R*, 3'*R*)-(*P*, *P*)-*trans*-**6a** [21] allowed the realization of the first light-powered molecular motor in which repetitive unidirectional 360° rotary motion was achieved [9].

The exploitation of the following two fundamental principles was the key to success:

- i. Photochemical *trans*–*cis* isomerization around a carbon–carbon double bond is usually a very fast and energetically uphill process in nature [22].
- ii. 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 [5].



When we examine the structure of **6** it is easily recognized that both a stereogenic center, with fixed stereochemistry, and a helical structure, the helicity of which can be changed by photoisomerization, are present in the same molecule. Another important feature of this system is that the methyl substituents can adopt two distinct orientations. This results in two distinct forms; the molecular structures and conformations are shown in Fig. 5. In the more stable (3*R*, 3'*R*)-(*P*, *P*)-*trans*-**6a** the methyl substituents adopt an axial orientation, whereas in the unstable (3*R*, 3'*R*)-(*M*, *M*)-*trans*-**6d** the methyl substituents are in an equatorial orientation. MOPAC93-AM1 calculations show that the differ-

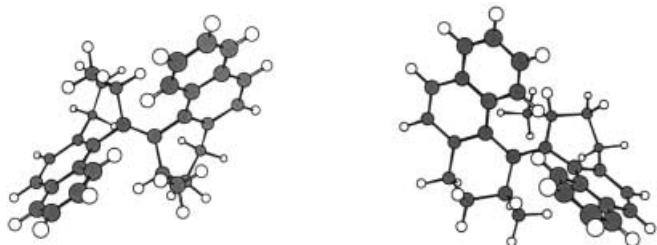
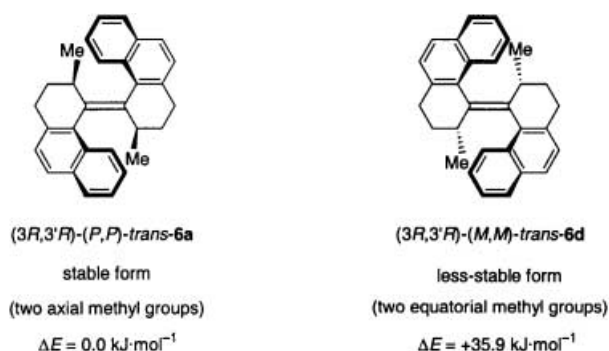
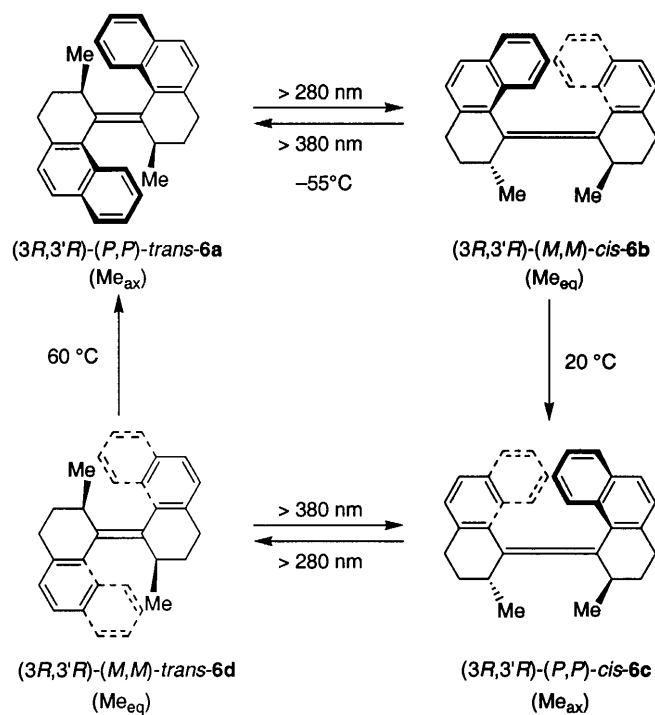


FIGURE 5 Molecular structure of **6a** and **6d**

ence in stability (35.9 kJ mol^{-1}) is due to steric hindrance of the methyl groups in the unfavorable equatorial orientation. A difference in stability of 46.0 kJ mol^{-1} was found for the stable and unstable forms of the corresponding *cis*-isomers.

The photochemical and thermal isomerization processes are summarized below. Photochemical isomerization ($\lambda > 280 \text{ nm}$) of $(3R, 3'R)$ - (P, P) -*trans*-**6a** at -55°C provides $(3R, 3'R)$ - (M, M) -*cis*-**6b** (10 : 90 ratio), which converts in an irreversible step into $(3R, 3'R)$ - (P, P) -*cis*-**6c** at room temperature. When a solution of $(3R, 3'R)$ - (M, M) -*cis*-**6c** is irradiated at the same wavelength $(R, 3'R)$ - (M, M) -*trans*-**6d** is formed and subsequent heating at 60°C induces an irreversible thermal isomerization exclusively to the starting compound $(3R, 3'R)$ - (P, P) -*trans*-**6a**. A cycle is shown with four distinct states that can be populated depending on the temperature and the wavelength of irradiation. At higher temperature ($> 60^\circ\text{C}$) all isomerization processes occur, resulting in continuous 360° rotary motion as long as the system is irradiated. The different isomers could be readily detected by NMR and UV spectroscopy. The chirality at each state and the directionality of the rotary motion were assigned by CD spectroscopy (Fig. 6). The modulation of the CD absorption at 217 nm (Fig. 6, inset) is characteristic of repetitive unidirectional rotation around the central carbon-carbon bond in **6**.



Although light energy is necessary to power this motor, the unidirectional rotation is governed by the methyl substituents. Photochemical *trans*-*cis* isomerization (step 1) of stable $(3R, 3'R)$ - (P, P) -*trans*-**6a** to unstable $(3R, 3'R)$ - (M, M) -*cis*-**6b** not only results in helix inversion, but forces the methyl substituents to adopt an unfavorable equatorial orientation. When the rotary motion in the molecule is continued in the same direction (step 2) by thermal interconversion into stable $(3R, 3'R)$ - (P, P) -*cis*-**6c**, strain is released and the methyl

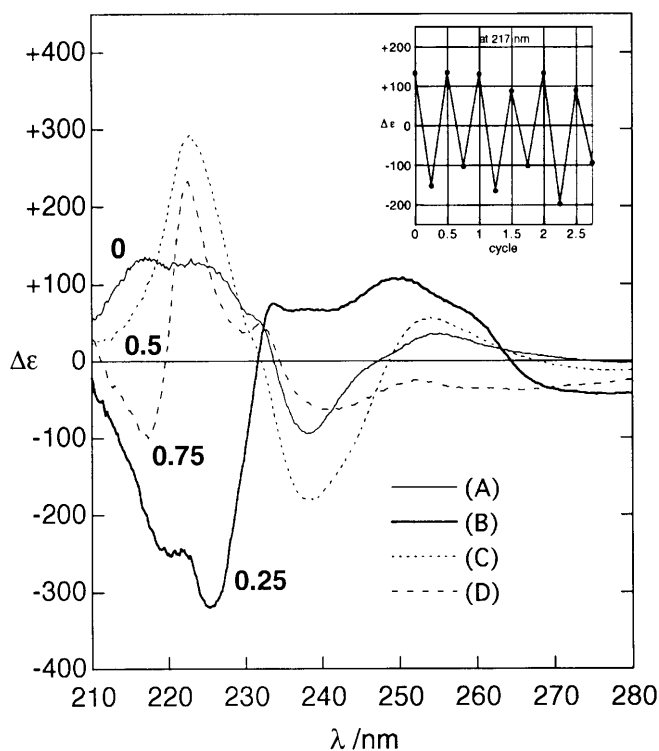


FIGURE 6 Circular dichroism spectra of each of the four stages of rotation. Trace A, $(3R, 3'R)$ - (P, P) -*trans*-**6a**, Trace B, $(3R, 3'R)$ - (M, M) -*cis*-**6b**, Trace C, $(3R, 3'R)$ - (P, P) -*cis*-**6c**, Trace D, $(3R, 3'R)$ - (M, M) -*trans*-**6d**. Numbers indicate part of rotary cycle completed. Inset, changes in $\Delta\epsilon$ value during three full rotation cycles monitored at 217 nm

substituents again adopt a more favorable axial orientation. In step 3 of the cycle the photochemical isomerization of stable $(3R, 3'R)$ - (P, P) -*cis*-**6c** into unstable $(3R, 3'R)$ - (M, M) -*trans*-**6d** once again forces the methyl substituents into the unfavorable equatorial orientation. The final thermal step restores the original stable isomer $(3R, 3'R)$ - (P, P) -*trans*-**6a** with the axially oriented methyl group. The Brownian ratchet mechanism involved in this system is also evident when one considers the relative energy levels as a function of the 360° rotation cycle as shown in Fig. 7. The re-

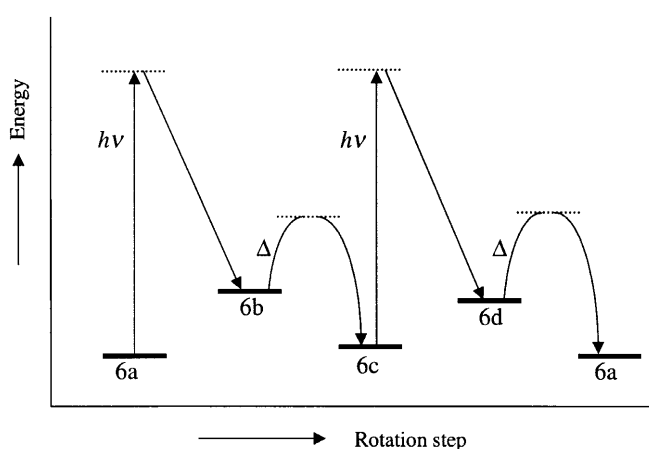


FIGURE 7 Relative energy profile of a 360° rotation cycle of **6a** comprising two photochemical and two thermal steps

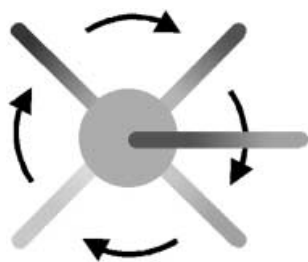


FIGURE 8 Schematic representation of unidirectional rotary motion

verse of the thermal isomerization steps (**6b** to **6c** and **6d** to **6a**) are effectively blocked while the forward steps are possible due to light excitation (photoisomerization) of the molecule. It should be emphasized that although one-half of the molecule undergoes a ratchet-type rotation with respect to the other half, the entire motor molecule is still experiencing the random thermal Brownian motion in solution. In summary, one full cycle comprises four steps where each light-driven energetically uphill step is followed by a thermal energetically downhill step. When one-half of the molecule is considered the stator (Fig. 8) the other half (the rotor part) undergoes a repetitive 360° rotation exclusively in a clockwise sense. It should be emphasized that clockwise or counterclockwise rotation simply depends on the choice of enantiomer [(*P,P*)-**6** or (*M,M*)-**6**, respectively] of the motor.

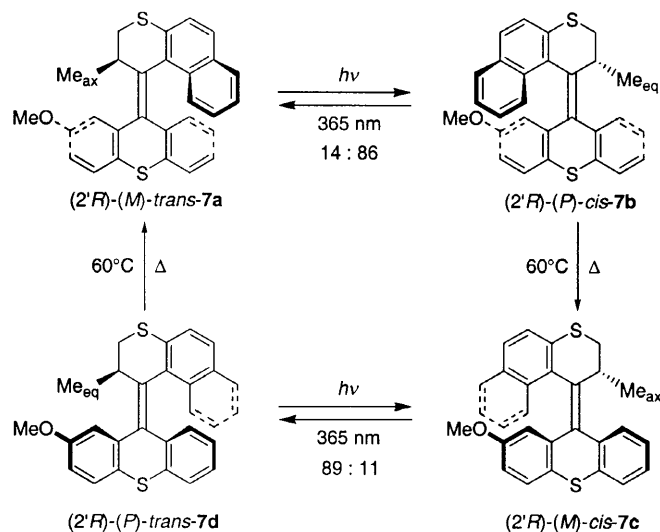
1.5 Second-generation molecular motor

Contemplating the construction of molecular machinery or the incorporation of the light-driven motor into multifunctional systems, we realized that the structure of **6**, featuring identical upper and lower halves, was less suitable for such endeavor. In the redesign of our motor we focussed on systems with distinct upper and lower halves, in which the lower part can be used for connection to other molecules or surfaces while the upper part still acts as a rotor, as illustrated in Fig. 9 [23].

The second-generation motor **7** contains a (*2'R*)-methyl-2,3-dihydronaphthopyran upper part and 2-methoxy-thioxanthene lower part. The molecular structure of stable (*2'R*)-(*M*)-*trans*-**7a**, determined by X-ray analysis, shows that the methyl substituent again adopts the more favorable axial orientation (Fig. 10). In contrast the structure of unstable (*2'R*)-(*P*)-*trans*-**7d** features an equatorial orientation of the methyl group. The different stereoisomers and the dynamic processes that are observed starting with (*2'R*)-(*M*)-*trans*-**7a** are shown.

Four distinct states are again observed and two photochemical and two thermal steps add up to a full 360° rotation cycle. The CD spectra after each isomerization step clearly show the distinct changes in helicity. The inset of Fig. 11 shows the changes of the $\Delta\varepsilon$ value at 272 nm as monitored during three full cycles, clearly demonstrating the repetitive and unidirectional nature of the rotary motion that was induced. Once again in the two thermal isomerization steps (steps 2 and 4 in Scheme 7) the *2'*-methyl substituent in **7** adopts the more favorable axial orientation and as a consequence the reverse-rotation pathway is effectively blocked.

Comparing this motor with the first-generation molecular motor (see above) it is remarkable that the presence of a single stereocenter and the change in orientation of one small methyl group is a sufficient condition to achieve unidirectional rotation.



In this motor the upper (naphthothiopyran) part undergoes a full 360° rotation around the central carbon–carbon double bond in a counterclockwise direction relative to the lower (thioxanthene) part at the appropriate wavelength (365 nm) and temperature (60°C).

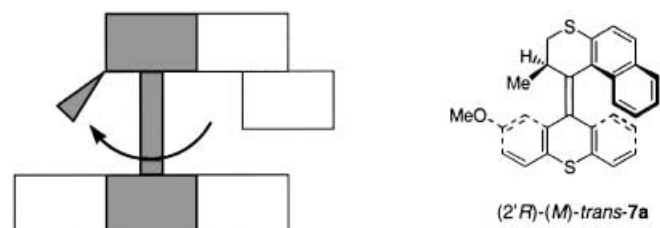


FIGURE 9 Second generation light-driven molecular motor

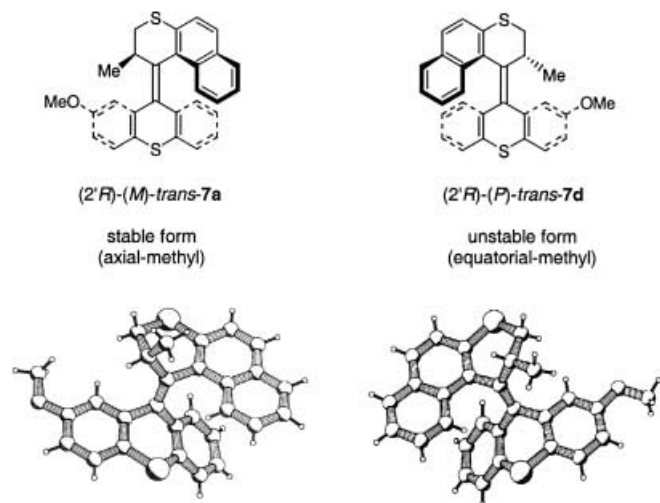


FIGURE 10 Molecular structure of **7a** and **7d**

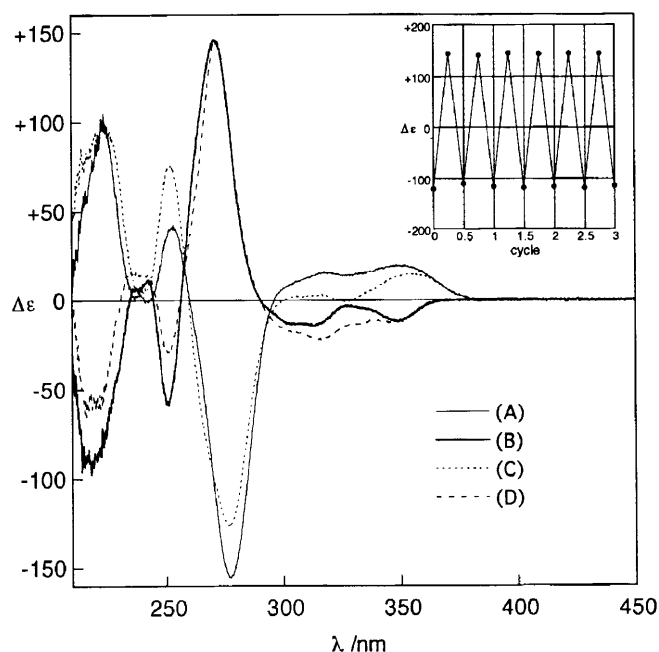


FIGURE 11 CD spectra of each of the four stages of rotation. Trace A, (2'R)-(M)-trans-7a; Trace B, (2'R)-(P)-cis-7b; Trace C, (2'R)-(M)-cis-7c; Trace D, (2'R)-(P)-trans-7d. Inset, changes in $\Delta\epsilon$ value during full rotation cycle monitored at 272 nm

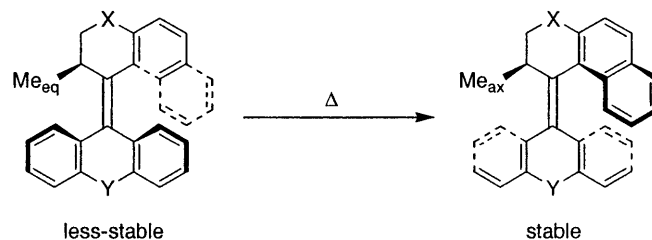
1.6 Tuning the speed of the rotary motion

The rotary motion comprises two photochemical and two thermal isomerization steps. Based on the extremely fast *cis*–*trans* alkene photoisomerization in the process of vision [24] and the fast isomerization (< 300 ps) in a number of symmetrically overcrowded alkenes as detected by femtosecond spectroscopy [25], it is safe to assume that the photoisomerization steps in the present systems will also be fast processes. The rate of the rotary motion is governed by the activation energy of the two thermal isomerization steps. Kinetic experiments revealed that the highest thermal isomerization barrier in motor 7 was already lowered by approximately 6.3 kJ mol^{-1} compared to that in the first-generation motor 6.

The approach we followed to tune the activation energies of the thermal steps involves the systematic modification of the bridging X and Y atoms in the upper and lower parts, respectively.

A smaller bridging atom X or Y reduces the steric hindrance in the so-called “fjord region” of the molecule [26]. This enables the upper and lower halves to slip along each other more easily. On the contrary, larger bridging atoms X and Y force the upper and lower halves toward each other, increasing the barrier for passage. For instance the presence of the smaller oxygen bridge (Y = O) in 9 compared to the sulfur bridge (Y = S) in 8 reduces the thermal barrier for helix inversion by 5.1 kJ mol^{-1} . A more pronounced effect is seen when X is altered. By changing from X = S (8) to X = CH₂ (10) the half-life for the thermal isomerization step could be decreased from 215 h to 40 min at room temperature [27]. With a better understanding of the delicate balance between ground-state distortion in these

systems and the steric and electronic effects on photochemical and thermal isomerization processes, as revealed by kinetic studies, we will be able to tune the rotary speed at will.



	$\Delta^\ddagger G^\theta$ (kJ·mol ⁻¹)	$t_{1/2}^a$ (h)
8: X = S, Y = S	105.7	215
9: X = S, Y = O	100.6	26.3
10: X = CH ₂ , Y = S	91.6	0.67 (40 min)

a: at room temperature (25 °C)

2 Conclusions and prospects

The molecular switches and motors discussed here provide the first stepping stones on a long and windy path to construct nanomachinery from molecules. Using the exquisite control of molecular chirality in combination with light as the energy source, we were able to achieve clockwise or counterclockwise rotary motion in the molecular switches, simply by changing the wavelength of the light used, as well as repetitive 360° unidirectional rotation in the molecular motors. Using molecular design and building principles from organic synthesis, the fundamental property of a molecular motor, i.e. energy consumption resulting in unidirectional rotary motion, was demonstrated by experiment. It is tempting to speculate on how to use these motors to overcome Brownian motion or to power molecular devices. To meet these challenges first we will have to develop methodologies to assemble the motors onto surfaces or connect them to other molecules. Alternatively, the motors might be embedded in membranes, this being the case with many of their natural counterparts. Matrix influences will certainly play an important role, as has already been observed with chiroptical switches bound to polymer films [28]. The second-generation molecular motors (Fig. 8) allow the introduction of ‘legs’ at the lower part to enable connection to the outer world without interfering with the propeller motion of the upper part. Experimental approaches toward this goal are in an advanced stage. The controlled movement of molecules or the construction of nanomechanical devices using such motors are fascinating long-term challenges, but the direction in which to move ahead is not random anymore.

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