

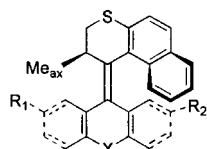
Light-Driven Molecular Rotor: Unidirectional Rotation Controlled by a Single Stereogenic Center

Nagatoshi Koumura, Edzard M. Geertsema, Auke Meetsma, and Ben L. Feringa*

Department of Organic and Molecular Inorganic Chemistry
Stratingh Institute, University of Groningen, Nijenborgh 4
9747 AG Groningen, The Netherlands

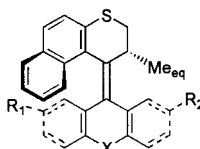
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Controlled motion by the conversion of chemical energy into mechanical energy is a key feature of living organisms¹ and recent studies on biomolecular motors² not only revealed fascinating structures and functions but also offered a formidable challenge for the bottom-up construction of molecular motors.³ A number of systems have been designed in which movement or change in shape occurs in response to external-chemical, electrochemical, or photochemical stimuli.⁴ Recently Kelly et al.⁵ and Harada, Feringa, and co-workers⁶ reported the first examples of unidirectional rotary motion in molecular type motors. In our initial design⁶ helical shaped overcrowded alkenes (biphenanthrylidene)s,⁷ featuring identical chiral upper and lower halves, were used. Two photochemical *trans*–*cis* isomerizations are each followed by a thermal irreversible helix inversion and the 4-step cycle completes a full 360° rotation process. We envisioned that in the next stage toward molecular machinery the construction of rotor type molecules with distinct upper and lower halves as well as tuning of the helix inversion steps by structural modifications had to be addressed.



stable forms (pseudo-axial methyl)

(2'R)-(M)-*trans*-1: X=S, R₁=OMe, R₂=H
(2'R)-(M)-*cis*-2: X=S, R₁=H, R₂=OMe
(2'R)-(M)-5: X=S, R₁=R₂=H
(2'R)-(M)-7: X=S, R₁=R₂=OMe
(2'R)-(M)-9: X=O, R₁=R₂=H



unstable forms (pseudo-equatorial methyl)

(2'R)-(P)-*trans*-3: X=S, R₁=H, R₂=OMe
(2'R)-(P)-*cis*-4: X=S, R₁=OMe, R₂=H
(2'R)-(P)-6: X=S, R₁=R₂=H
(2'R)-(P)-8: X=S, R₁=R₂=OMe
(2'R)-(P)-10: X=O, R₁=R₂=H

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Here we wish to report a second generation of unidirectional light-driven molecular rotors, the adjustment of the thermal isomerization barriers, and the remarkable finding that the presence of a single stereogenic center is sufficient to control unidirectional rotary motion.

The new type of molecular rotor contains a chiral 2-methyl-2,3-dihydrothiopyran upper part and a (thio)xanthene lower part. The overcrowded alkenes were prepared by diazo–thioetone coupling⁸ and a subsequent desulfurization using copper powder.⁹ *Trans*-1 and *cis*-2 were separated by HPLC on silica gel (hexane: EtOAc = 50:1) and detailed ¹H NMR analysis, molecular modeling studies,¹⁰ and X-ray analysis of *trans*-1 (Figure 1) resulted in the assignment of the geometrical isomers¹¹ and revealed the preferred conformation of the molecules. In particular the coupling constants of H(2') and H(3') of 7.3 and 2.9 Hz (*trans*-1) and 7.3 and 3.3 Hz (*cis*-2), respectively, prove that the methyl groups at the 2'-position of both isomers adopt a pseudoaxial orientation.

Enantioresolution of both isomers was independently achieved by chiral HPLC (Chiralpak OD, heptane:2-propanol = 99:1). The absolute configuration of [CD(–)277.2]-*trans*-olefin 1 was unequivocally determined to be (2'R)-(M) by X-ray diffraction (Figure 1). The CD spectrum of (2'R)-(M)-*trans*-1 exhibits intense Cotton effects (Figure 2).¹²

Irradiation¹³ of (2'R)-(M)-*trans*-1 in *n*-hexane at 365 nm and 10 °C resulted in the formation of (2'R)-(P)-*cis*-4, with the methyl group at the 2'-position adopting an equatorial orientation as determined by ¹H NMR.¹⁴ A (2'R)-(P)-*cis*-4 to (2'R)-(M)-*trans*-1 ratio of 86:14 was observed. This photochemical *trans*–*cis* isomerization induced an *M* to *P* helicity inversion which was detected by CD measurement (Figure 2, trace A to B). When the temperature of the solution of (2'R)-(P)-*cis*-4 was raised to 60 °C, a complete conversion to (2'R)-(M)-*cis*-2 was observed and the concomitant change in CD absorption showed the helix reversal, from *P* to *M* helicity, associated with this thermal interconversion (Figure 2, trace B to C). Subsequent irradiation¹³ of (2'R)-(M)-*cis*-2 in *n*-hexane (10 °C) at 365 nm resulted in formation of (2'R)-(P)-*trans*-3 with the methyl group at the 2'-position again in an equatorial orientation as determined by ¹H NMR.¹⁵ A (2'R)-(P)-*trans*-3 to (2'R)-(M)-*cis*-2 ratio of 89:11 was observed and the change in CD absorption that accompanies this photochemical *cis* to *trans* isomerization is due to simultaneous *M* to *P* helicity reversal (Figure 2, trace C to D). When the temperature of the solution of (2'R)-(P)-*trans*-3 was increased to 60 °C, a complete conversion to (2'R)-(M)-*trans*-1 was observed and the CD absorption again changed sign (Figure 2, trace D to A). The inset of Figure 2 shows the change of Δε value at 272 nm as monitored during three full cycles clearly demonstrating the repetitive nature of the rotary motion that can be induced.¹⁶ The X-ray structural analysis of (2'R*)-(P*)-*trans*-3 confirmed that the methyl group at the 2'-position adopts an equatorial

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(11) The ¹H NMR spectra of *trans*-1 and *cis*-2 are remarkably different and the absorption of the methoxy group is shifted from 3.86 ppm (*trans*-1) to 3.01 ppm (*cis*-2) due to shielding by the naphthalene moiety in *cis*-2.

(12) (2'R)-(M)-*trans*-1: UV (*n*-hexane) λ_{max} 325 (ε 8300), 259 (35100), 222 (51300); CD (*n*-hexane) λ_{ext} 349.8 nm (Δε +19.1), 318.6 (+15.4), 277.2 (–155.4), 253.0 (+40.8), 223.8 (+98.1).

(13) Irradiation was performed with a 180 W high-pressure mercury lamp using a 365 nm filter (bandwidth = 10 nm, Ø = 5 cm) (1, 2, 9) or Pyrex filter (5, 7). Irradiation time is concentration dependent: 1 h for UV concentrations (3.0 × 10^{–5} M) and 12 h for NMR concentrations (2.0 × 10^{–3} M).

(14) Coupling constants for H(2') and H(3') of *cis*-4 are 12.4 and 7.3 Hz and the methoxy group shifted upfield to 2.99 ppm.

(15) Coupling constants for H(2') and H(3') of *trans*-3 are 12.1 and 7.3 Hz and the methoxy group shifted downfield to 3.85 ppm.

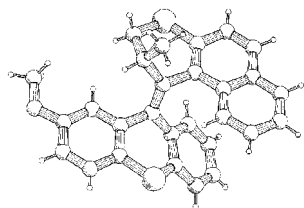


Figure 1. PLUTO drawing of $(2'R)$ - (M) -*trans*-1.

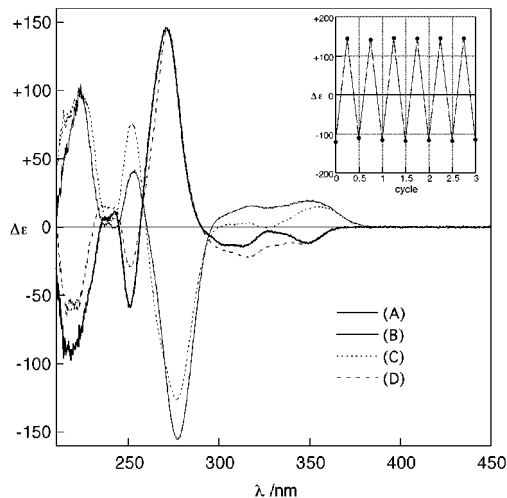


Figure 2. Circular dichroism spectra of each of the four stages of rotation: Trace A, $(2'R)$ - (M) -*trans*-1; Trace B, $(2'R)$ - (P) -*cis*-4; Trace C, $(2'R)$ - (M) -*cis*-2; Trace D, $(2'R)$ - (P) -*trans*-3. Inset, changes in $\Delta\epsilon$ value during a full rotation cycle monitored at 272 nm.

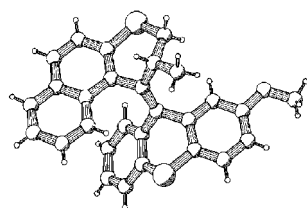


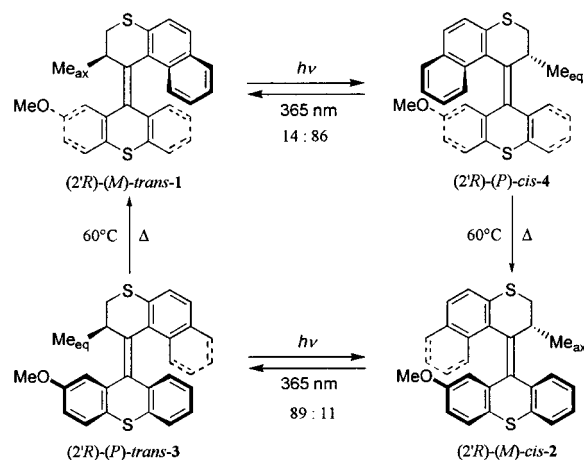
Figure 3. PLUTO drawing of racemic $(2'R^*)$ - (P^*) -*trans*-3.

orientation in accordance with the results of the ^1H NMR study (Figure 3).

Scheme 1 shows the different stereoisomers and the dynamic processes that are observed starting with $(2'R)$ - (M) -*trans*-1. The experimental results show that the upper naphthothiopyran moiety undergoes a full 360° rotation in a counterclockwise sense relative to the lower thioxanthene part. Two photochemical conversions, which are both energetically uphill processes, induce rotations around the central double bond and generate the less stable isomers $\{(2'R)$ - (P) -*cis*-4 and $(2'R)$ - (P) -*trans*-3}. Each photochemical step is followed by an energetically downhill process generating the more stable isomers $\{(2'R)$ - (M) -*cis*-2 and $(2'R)$ - (M) -*trans*-1}. In the two thermal steps the $2'$ -methyl-substituent adopts the more favorable axial orientation and the reverse rotation pathway is effectively blocked. At the appropriate wavelength (365 nm) and temperature (60°C), a continuous unidirectional rotation is induced in the system. Compared to the original molecular rotor, based on biphenanthrylidene,⁶ it is remarkable that the presence of a single stereogenic center ($C(2')$) is a sufficient condition to accomplish unidirectional rotation.

(16) After three cycles a mixture of *trans*-1/*cis*-2 with a ratio of 6/4 is observed due to the photoequilibria.⁹ However, this does not affect the repetitive unidirectional behavior of the molecules and each photochemical and thermal step still implies a helix inversion.

Scheme 1



The rotation rate is governed by the activation energy of the two thermal isomerization steps. To tune the activation energies of the thermal pathways three related molecules **5**, **7**, and **9**, which have different lower parts, were synthesized.⁹ Irradiation¹³ of toluene- d_8 solutions of olefins **5** and **7**, which have symmetric thioxanthene lower parts, resulted in the formation of unstable forms **6** (ratio **5**:**6** = 8:92) and **8** (ratio **7**:**8** = 13:87), respectively, with the methyl group at the $2'$ -position adopting an equatorial orientation. Irradiation¹³ of **9**, with a symmetric xanthene lower part, yielded the unstable form **10** with an equatorial methyl group in a 23:77 ratio. Since these molecules have symmetric lower parts, heating of the unstable forms **6**, **8**, and **10** resulted in complete conversion to their respective starting olefins **5**, **7**, and **9**. ^1H NMR studies in the range 35 – 65°C revealed first-order kinetics for the conversions of **6** to **5** and **8** to **7**, and E_a values of 24.9 and 24.2 kcal/mol were found, respectively. These results show that methoxy substituents ($R_1, R_2 = \text{OCH}_3$) at the lower half of the molecule do not influence the activation energy drastically and compared to the biphenanthrylidene molecular rotor⁶ we succeeded in lowering the thermal barrier by approximately 1.5 kcal/mol. A further decrease of the thermal barrier for helix inversion by 2 kcal/mol was achieved with **9** featuring a xanthene lower part. The activation energy of 22.7 kcal/mol, found for the conversion of **10** to **9**, implies that changing the bridging heteroatom X at the lower part from sulfur to oxygen reduces the steric hindrance in the “fjord region” of the molecule resulting in more favorable thermal helix inversion steps (Scheme 1).

In conclusion a new type of molecular motor with a distinct upper and lower half—a feature essential for coupling the rotor unit to e.g. a surface—showing unidirectional rotation controlled by a single stereocenter was developed. Relative to the bottom part (the stator) the upper propeller unit undergoes a repetitive 360° rotation in four distinct steps with light of the appropriate wavelength and it was shown that the energy barriers for the thermal steps in the rotary motion can be adjusted by structural modification.

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Supporting Information Available: Experimental details and X-ray structural information (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.