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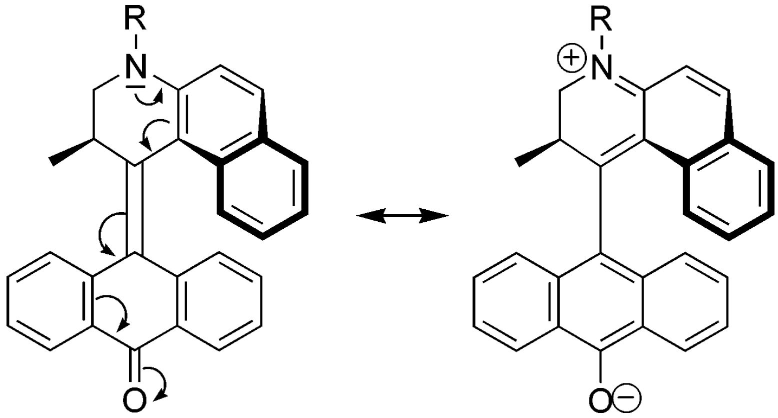

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Acceleration of a Nanomotor: Electronic Control of the Rotary Speed of a Light-Driven Molecular Rotor

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Facing the challenge to construct nanoscale machines, it has been noted that molecular motors stand out as essential components to provide power to such systems.[1] The diversity of fascinating biological motors, such as the kinesin or myosin linear and ATP-ase rotary motor systems,[2] has been a source of inspiration for the development of artificial molecular mechanical devices (such as switches, shuttles, and muscles)[3] and a variety of elegant rotor systems.[4] The sterically overcrowded alkenes prepared in our laboratories provided the basis for a light-driven motor.[5,6] Unidirectional rotation is achieved by a combination of a photochemically mediated *cis*−*trans* isomerization followed by an irreversible thermal isomerization.[6] The motor described here is based on the second-generation light-driven unidirectional molecular motors **1**.[7] A limitation of these molecular motors proved to be their low rotary speed. A major goal of our molecular motor program is to substantially lower the Gibbs energy of activation of the thermal isomerization, the rate-determining step for the 360° rotation around the central double bond in these overcrowded alkenes. Thus far, all attempts to decrease the thermal isomerization barriers have involved structural modifications in order to diminish steric interactions around the *fjord region* of the molecules. This has been achieved by the introduction of smaller-sized atoms in **1** at bridging position X or using smaller rings appended to the central alkene.[8]

Herein we report a substantial electronic effect on the thermal isomerization around the central double bond (the axis of rotation), which results in a remarkable increase of the rate of thermal isomerization. We designed a new second-generation motor (Figure 1), with an amine moiety in the upper half, the lone pair electrons of which can be delocalized by direct conjugation with a ketone functionality in the lower half of the molecule. This electronic push−pull system was anticipated to generate a large polarizing effect on the central olefinic bond[9] evident from a resonance structure with a single bond as the central axis of the rotor. The *N*-Boc protecting group in **2** (Figure 2), introduced for synthetic reasons, was found to be essential for the stability of the motor during the irradiation experiments.[10] Synthesis of the overcrowded alkenes **2** and **3** was achieved by diazo-thioketone coupling of the upper and lower halves as a key step, followed by desulfurization using triphenylphosphine.[11] Racemic *cis*-**3** and *trans*-**3**, with a nonsymmetric lower half, were separated by column chromatography on silica (hexane:EtOAc = 16:1), and the structure of *trans*-**3** was unequivocally assigned by single-crystal X-ray analysis (Figure 2).[11,12] Enantioresolution was achieved by CSP−HPLC (Chiralpak AD, heptane:2-propanol = 90:10).[13]

The photoisomerization of (2′*R*)-(*M*)-**2** was followed using UV/vis and circular dichroism (CD) spectroscopy (Figure 3). A sample of (2′*R*)-(*M*)-**2** in *n*-hexane was irradiated at −10 °C using a high-pressure Hg lamp ($\lambda > 280$ nm), resulting in the appearance of a broad absorption around 450 nm in the UV/vis spectrum (showing positive solvatochromism[11,14]) and a change in sign of the major CD absorptions, indicative of the helix inversion of the molecule to provide (2′*R*)-(*P*)-**2**.[15] On the basis of the change in the CD spectrum, a (2′*R*)-(*M*)-**2**:(2′*R*)-(*P*)-**2** ratio of 35:65 was established at the photostationary state[16] (supported by ^{1}H NMR measurements at −75 °C[11]).

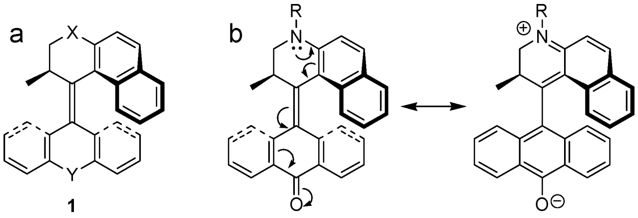
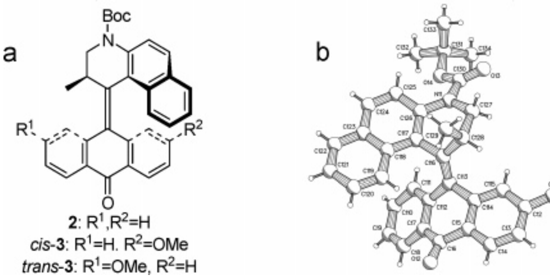


Figure 1. (a) The second-generation light-driven molecular motor **1** and (b) the proposed push−pull electronic effect on the central olefin.



2: R^1,R^2=H
cis-**3**: R^1=H, R^2=OMe
trans-**3**: R^1=OMe, R^2=H

Figure 2. (a) New motors **2** and **3**; (b) Pluto drawing of racemic *trans*-**3** (one enantiomer shown; this structure does not express the absolute stereochemistry of the molecule).

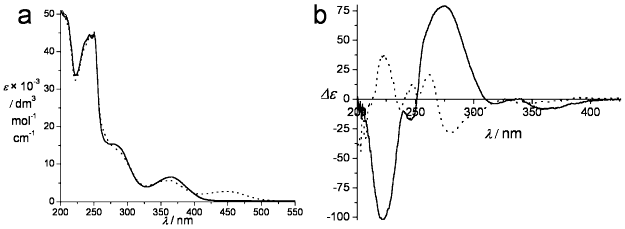


Figure 3. (a) UV/vis and (b) CD spectra (*n*-hexane) of stable (2′*R*)-(*M*)-**2** (solid line) and the photostationary state mixture with (2′*R*)-(*M*)-**2** and (2′*R*)-(*P*)-**2** (dotted line) after irradiation ($\lambda > 280$ nm).

Upon standing in the dark for 30 min at 20 °C, the spectra corresponding to the stable isomer (2′*R*)-(*M*)-**2** were fully restored. The kinetics and thermodynamic parameters of the thermal helix inversion of (2′*R*)-(*P*)-**2** to (2′*R*)-(*M*)-**2** were determined by monitoring the CD signal at 274 nm in the dark over a range of temperatures: $\Delta^{\ddagger}G^{\circ} = 81.7$ kJ·mol^{-1} ($\Delta^{\ddagger}H^{\circ} = 72.1$ kJ·mol^{-1}, $\Delta^{\ddagger}S^{\circ} = -32.9$ J·mol^{-1}·K^{-1}, $t_{1/2}$(20 °C) = 40 s).[11]

Motor molecule **2** contains a symmetric lower half, and as such, just one photochemical and one thermal isomerization step, each accompanied by a helix inversion, convert the olefin to its initial stable isomer. To be able to identify the four distinct steps that

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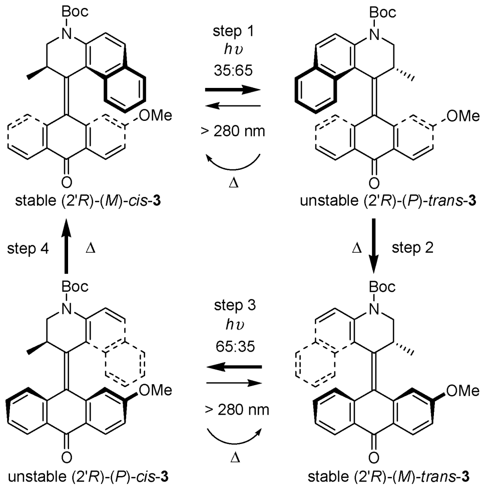
Scheme 1. Photochemical and Thermal Isomerizations for **3**



define a full 360° rotary cycle of the upper half with respect to the lower half, as shown in Scheme 1, a methoxy substituent was introduced, and the rotation cycle of olefin **3** was followed with low-temperature ^{1}H NMR spectroscopy.

Upon irradiation of a racemic mixture of *cis*-**3** (365 nm, 5 h, −80 °C), new signals corresponding to the unstable *trans* isomer appeared.[11] The signals for the methyl substituent (doublets at 0.06 and 0.19 ppm), which adopts an axial orientation in the stable *cis*-**3** isomer, shift downfield (0.67 and 0.82 ppm) as a result of the equatorial orientation which it adopts in this unstable *trans*-**3** isomer.[17] Also, the signals for the methoxy group (singlets at 2.47 and 2.63 ppm) shifted to considerably lower field (2.92 and 3.22 ppm) due to the *cis*-to-*trans* isomerization. On standing for 30 min at 20 °C in the dark, conversion of the unstable *trans*-**3** to the expected stable *trans*-**3** isomer with an axial methyl group (0.13 and 0.18 ppm) was observed. Examination of the integrals reveals that not all unstable *trans*-**3** is converted to stable *trans*-**3**: notably, 20% is thermally converted back to stable *cis*-**3**. Similar experiments starting with racemic *trans*-**3** indicate a corresponding *trans*-to-*cis* isomerization.[11]

When the thermal and photoisomerizations of enantiomerically pure **3** (*cis* and *trans*) were investigated with UV/vis and CD spectroscopy, results similar to those found for **2** were observed.[11] The following activation parameters were determined: $\Delta^{\ddagger}G^\circ = 84.7$ kJ·mol^{-1} ($\Delta^{\ddagger}H^\circ = 67.4$ kJ·mol^{-1}, $\Delta^{\ddagger}S^\circ = -59.1$ J·mol^{-1}·K^{-1}, $t_{1/2}$(20 °C) = 124 s) for the conversion of unstable (2′*R*)-(*P*)-*trans*-**3** to the stable isomers, $\Delta^{\ddagger}G^\circ = 85.1$ kJ·mol^{-1} ($\Delta^{\ddagger}H^\circ = 59.3$ kJ·mol^{-1}, $\Delta^{\ddagger}S^\circ = -88.1$ J·mol^{-1}·K^{-1}, $t_{1/2}$(20 °C) = 173 s) for the conversion of unstable (2′*R*)-(*P*)-*cis*-**3** to the stable isomers.[18]

The new molecular motor is significantly faster than all previously described systems. The two photochemical and two thermal isomerizations (Scheme 1) observed for **3** by low-temperature CD and ^{1}H NMR spectroscopy confirm the four-stage rotary cycle and the unidirectionality of the 360° rotary motion for new motors **2** and **3**. While an *N*-Boc-protected amine has a smaller electron-donating capability compared to that of the *N*-alkyl group initially proposed, it is clearly still significant,[19] giving greater single bond character to the rotational axis in the unstable form.[20,21] It should be emphasized that the observation that the thermal steps do not result in exclusively a "forward" helix inversion, but also involve a 20% "backward" *cis*−*trans* isomerization, leaves the overall unidirectionality intact, as steps 2 and 4 are strictly unidirectional.[22] Compared to earlier generation motors,[6−8] the increase in speed, which allows for full rotation at 20 °C at the scale of minutes instead of hours, is a major advance and offers perspectives for future applications of these light-driven motors.

Supporting Information Available: Synthetic procedures and the experimental and analytical details, spectral and kinetic data, X-ray structural information (PDF) and the crystallographic information file (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) See Supporting Information.
(12) Bond length of the central olefin was 1.352 Å (comparable to other motors).
(13) Assignment of the absolute configuration was based on comparison of CD data with those of related compounds (see ref 7).
(14) The positive solvatochromism of the long-wavelength band of the unstable isomer indicates intramolecular charge transfer nature for the corresponding transition. Related push−pull stilbene systems show similar CT bands. See: Meier, H.; Gerold, J.; Kolshorn, H.; Baumann, W.; Bletz, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 292−295.
(15) Quantum yield = 0.12 (determined in the 5−10% range of photoisomerization).
(16) For previous systems, the photoequilibria favor the unstable isomer. Whereas the rate of rotation is almost solely determined by the thermal steps, the "photon-efficiency" is affected, as it is governed by a combination of quantum yield and photostationary state equilibrium.
(17) At low temperature, all signals of all isomers of **3** are split up, due to the fact that the rotation in the carbamate moiety is frozen out.
(18) Corrected for the thermal "backward" isomerization, $t_{1/2}$(20 °C) = 155 s for the (2′*R*)-(*P*)-*trans*-**3** conversion via step 2, $t_{1/2}$(20 °C) = 217 s for the (2′*R*)-(*P*)-*cis*-**3** conversion via step 4, and $t_{1/2}$(20 °C) = 50 s for the (2′*R*)-(*P*)-**2** to (2′*R*)-(*M*)-**2** conversion via the "forward" helix inversion.
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(20) Remarkably, the thermal barrier is significantly increased by the introduction of the methoxy substituent. A reasonable explanation for this observation is that the methoxy group is in conjugation with the carbonyl, thereby lowering its electron-withdrawing capabilities.
(21) An increased rate of the thermal steps was observed in more polar solvents, in accordance with a dipolar transition state. In CD$_3$OD, 58% of the unstable *trans* isomer was converted back to stable *cis*.
(22) The thermal helix inversion of stable (2′*R*)-(*M*)-*cis*-**3** to unstable (2′*R*)-(*P*)-*cis*-**3** and stable (2′*R*)-(*M*)-*trans*-**3** to unstable (2′*R*)-(*P*)-*trans*-**3** has never been observed (by NMR or CD).

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