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MHz Unidirectional Rotation of Molecular Rotary Motors

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Nature's ubiquitous use of functional molecular motors,¹ from the kinesin and myosin linear motors² to the ATPase and flagella rotatory motors,³ are testimony to the potential of molecular-based motor systems as functional components in future nanoscale devices.⁴ The efficiency of natural motors in converting chemical to kinetic energy and the rate at which these rotary motors can engage in repetitive unidirectional rotation sets a clear challenge for synthetic systems. Although chemically powered unidirectional rotation has been demonstrated recently,⁵ the most effective artificial systems developed thus far employ light to fuel rotary motion.^{4,6}

The molecular rotary motors we have developed in recent years display repetitive unidirectional rotation of a molecular rotor component relative to a stator component, connected via a C=C "axle", and use light to drive two photochemical cis–trans isomerization steps each of which is followed by an efficient unidirectional thermal helix inversion (Figure 1).⁷ As photochemical cis–trans isomerization occurs in only a few picoseconds,⁸ the overall rate of rotation is limited by the barrier to the thermal step, that is, the helix inversion in which the naphthyl component of the rotor slips over a phenyl ring of the stator unit. Through a variation of the X and Y groups⁹ and the stereogenic substituent⁶ (Figures 1 and 2) a million-fold increase in this rate was achieved, the maximum being 10² s^{−1} at room temperature. The size of the rotor bridging atom X was found to be directly related to the rate constant of thermal helix inversion due to its effect on steric crowding with the stator.^{7,9}

Here we demonstrate that cyclopentane-based molecular rotary motors, which display even less steric hindrance (Figure 2) can accomplish unidirectional rotary motion with MHz rotational frequencies at ambient temperatures. Direct measurement of the kinetics of the thermal helix inversion at ambient temperatures is achieved using transient absorption spectroscopy. The experimental data are in full agreement with extrapolated data obtained by cryogenic UV–vis and CD spectroscopic techniques and prove that these molecular motors display well-defined rotational behavior up to MHz frequencies over a wide temperature range.

The synthetic approach toward the new motors is based on methods described before,¹⁰ and their structures are shown in Figure 2. Irradiation of **1** in isopentane at temperatures between 150 and 180 K resulted in a photostationary state (PSS) consisting of stable and unstable **1**, for which the rate of thermal helix inversion could be measured by UV–vis spectroscopy. Analysis of these rates and subsequent extrapolation to 293.15 K yielded a barrier to thermal helix inversion $\Delta^\ddagger G_1$ of 57.9 kJ/mol ($t_{1/2} = 2.4$ ms). However, the minor differences between the UV–vis absorption spectrum of the stable form and the unstable form at the PSS together with poor solubility at 150 K precluded the use of this approach for the methoxy-desymmetrized motors **2**, so that the difference between the trans to cis and cis

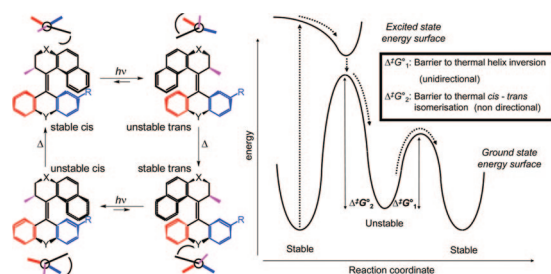


Figure 1. Four-step unidirectional rotary cycle (left) and free energy diagram (right).



Figure 2. Structures of molecular motors 1–6.

to trans pathways, reflecting unidirectionality, could not be established unequivocally.

An alternative approach to studying the fast thermal isomerization processes following the photochemical isomerization of these compounds is to use ns-pulsed laser transient absorption (TA) spectroscopy, a technique that is typically employed for probing photoexcited state dynamics, although it has also been used, for example, in probing ground-state intramolecular hydrogen transfer,¹¹ protein conformational changes,¹² or conformational analysis of bianthrone.¹³ As photochemical cis–trans isomerization occurs within several picoseconds, the excitation of these compounds using a pulsed laser (λ_{exc} , 355 nm; fwhm, 9 ns) generates a photoexcited state population, which on the time scale of the measurement results in instantaneous formation of a significant population of the unstable form. This allows for TA spectroscopy to be employed to follow the ground-state relaxation of the unstable isomer to the stable isomer. That is, the thermal helix inversion can be monitored in real time at ambient temperatures, circumventing the need to extrapolate from data obtained at low temperature.

For **1**, the ground-state transient UV–vis-absorption depletion at 350 nm is in perfect agreement with that of the difference between the UV–vis absorption spectra of the stable form and the PSS at 150 K (Supporting Information). Temperature dependent transient kinetic analysis provided a value of 57.1 kJ/mol for the barrier to thermal helix inversion $\Delta^\ddagger G_1$ ($t_{1/2} = 1.4$ ms), in good agreement with the value obtained by extrapolation of low temperature data. The unidirectionality of the rotation could be verified by kinetic analysis of the TA spectra of isomers **2**. At 26 °C, *cis*-**2** was converted via an unstable intermediate to a compound of higher molar absorptivity at 360 nm, that is, *trans*-**2** ($k_{\text{c-t}} = 399 \pm 8$ s^{−1}, $t_{1/2} = 1.9$ ms). Similarly, *trans*-**2**

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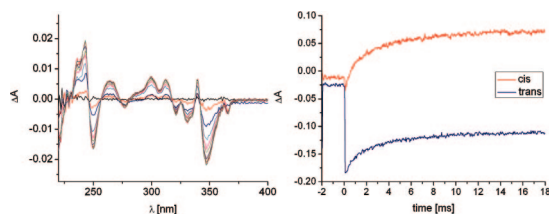


Figure 3. UV-vis-difference spectra of **1** (left) and TA traces for interconversion of *cis*-**2** and *trans*-**2** in toluene (right).

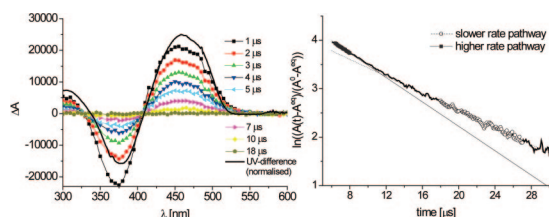


Figure 4. Transient and UV-vis difference spectra of **3** (left) and combined transient traces of *cis*/*trans*-**4** (55/45 ratio, right).

converted to *cis*-**2** via a different intermediate at a slower rate ($k_{t-c} = 378 \pm 7 \text{ s}^{-1}$, $t_{1/2} = 1.7 \text{ ms}$, Figure 3). Interconversion of *cis*-**2** and *trans*-**2** via two distinct pathways results in clear evidence for the unidirectionality of rotation of structures **1** and **2**, with a maximum rotation rate of 248 Hz for **1**.

The same approach was taken for **3** and the related compounds *cis*-**4** and *trans*-**4**.¹⁴ For **3**, irradiation at 120 K in isopentane: methylcyclohexane (3/1 v/v)¹⁵ resulted in full conversion to the unstable form. Analysis of the rate of thermal helix inversion by CD-spectroscopy in isopentane ($125 < T < 135 \text{ K}$) provided an activation barrier of 41.0 kJ/mol at 20 °C by extrapolation. TA spectra obtained at 26 °C in hexane are in excellent agreement with the difference spectrum between the stable form and its PSS obtained at 120 K (Figure 4). Analysis of the ns-TA decay kinetics of a mixture of *cis*/*trans*-**4** (55/45 ratio, 26 °C) showed that the rate of the thermal helix inversion process that follows the photochemistry is on a μs time scale.¹⁶ The biexponential character of the decay kinetics ($k_1 = 1.26(2) \times 10^5 \text{ s}^{-1}$ and $k_2 = 8.9(1) \times 10^4 \text{ s}^{-1}$) indicates that the relaxation from *cis*-unstable **4** to *cis*-stable **4** and *trans*-unstable **4** to *trans*-stable **4** show different thermal activation barriers. Although it cannot be unambiguously assigned which rate constant reflects the *cis* to *trans* or the *trans* to *cis* conversion, the results are in clear support of unidirectional rotation (Figure 4).

Compound **5** and the related isomers *cis*- and *trans*-**6** showed similar dynamic behavior as **3** and **4**, except for the rates of the different processes. The time scale of thermal (nonphotoinduced) *cis*–*trans* isomerization allowed for isolation of both the *cis*-**6** and *trans*-**6** isomers by flash column chromatography and cold evaporation, followed by crystallization.¹⁷

The UV-vis difference spectrum between the stable form and the PSS of **5** obtained in methylcyclohexane/methylcyclopentane (1/1 v/v)¹⁵ at 90 K is very similar to the TA spectrum obtained at 26 °C in CH_2Cl_2 . Analysis of the rate of thermal helix inversion of the photoinduced unstable form by direct measurement at ambient temperatures in CH_2Cl_2 and by extrapolation of data obtained in the range of 85–95 K by CD-spectroscopy in liquid propane solution gave comparable results, with the differences being attributable to the difference in solvent and the extrapolation over a large temperature region (Table 1). As in the case of **2**, the low solubility of the methoxy-substituted isomers **6** at $T < 120 \text{ K}$ prevented analysis of the *cis* to *trans* and *trans* to *cis* pathways. TA spectroscopy at ambient temperatures allowed the activation energy of conversion of unstable *cis*-**6** to stable *cis*-**6** and unstable *trans*-**6** to stable *trans*-**6** to be determined

Table 1. Barriers of Activation to Thermal Helix Inversion Obtained by (Left) Cryogenic UV-vis or CD Spectroscopy and Extrapolation and (Right) by TA Spectroscopy at 26 °C

	UV-vis/CD spectroscopy			TA kinetics	
	$\Delta^\ddagger G^\circ$ (kJ/mol)	k (s^{-1})	$t_{1/2}$ (s) (20 °C)	$\Delta^\ddagger G^\circ$ (kJ/mol)	$t_{1/2}$ (s) (20 °C)
1	57.9 ^a	2.9×10^2	2.4×10^{-3}	57.1 ^c	1.4×10^{-3}
3	41.0 ^a	3.0×10^5	2.3×10^{-6}	41.5 ^d	2.8×10^{-6}
5	35.8 ^b	2.6×10^6	2.7×10^{-7}	33.5 ^e	1.1×10^{-7}
<i>cis</i> - 6				35.0 ^e	1.9×10^{-7}
<i>trans</i> - 6				34.2 ^e	1.4×10^{-7}

^a Isopentane. ^b Propane. ^c Toluene. ^d Hexane. ^e CH_2Cl_2 .

($E_a = 21.0(8) \text{ kJ/mol}$ and $10.8(8) \text{ kJ/mol}$, respectively). The activation energies are sufficiently different to conclude that *cis*-**6**, when converted photochemically to unstable *trans*-**6**, undergoes isomerization to stable *trans*-**6** by a different pathway than the pathway followed when converting stable *trans*-**6** to stable *cis*-**6** via unstable *cis*-**6**, reflecting the unidirectionality of the process.

With the rate of thermal helix inversion at 20 °C being $6 \times 10^6 \text{ s}^{-1}$ for **6** and the unidirectionality demonstrated at ambient temperatures, we can conclude that this structure is capable of achieving unidirectional rotation at 3 MHz, at room temperature under suitable irradiation conditions.

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Supporting Information Available: Characterization of compounds **2** and **6**, detailed experimental procedures, transient spectra of **1**, **3**, and **5** and Arrhenius plots of **1**, **3**, **5**, and **6**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (17) The barriers for thermal isomerization $\Delta^\ddagger G^\circ_2$ were determined to be 107.7 and 106.9 kJ/mol respectively ($t_{1/2}$ (20 °C) = 20 d and 14.8 d).

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