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In control of the speed of rotation in molecular motors. Unexpected retardation of rotary motion†

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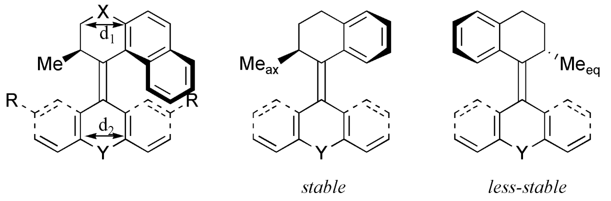
Surprisingly, a new motor with a tetrahydronaphthalene upper part rotates slower than the original molecular motor with a tetrahydrophenanthrene upper part despite decreased steric hindrance.

The challenge to design nanoscale machines[1] has stimulated chemists to construct mechanical molecular systems including switches,[2] motors,[3] shuttles[4] and muscles.[5] In order to be able to control linear and rotary movement at the molecular level insight into factors governing directionality and rate of molecular motions are essential. Recently we reported second generation light-driven molecular motors based on sterically overcrowded alkenes with a general structure as depicted in Fig. 1.[6,7] The key features of these second generation molecular motors **1**, containing a tetrahydrophenanthrene upper part, are the 360° unidirectional rotation around the central double bond involving two photochemical and two thermal steps. It was shown that the speed of rotation can be adjusted by variation of the bridging units X, in the upper part, and Y, in the lower part of the motor. The speed of rotation is directly correlated to the Gibbs energy of activation for the two irreversible thermal steps in the rotary process. Upon irradiation of the motor molecule in its more stable form (axial orientation of the methyl substituent as shown in **1**), a photoisomerisation takes place resulting in a helix inversion whereas the methyl substituent adopts a less stable equatorial conformation. In order to revert to the more favored conformation, the naphthalene unit of the upper part in **1** needs to pass along the lower part of the molecule, again with simultaneous helix inversion. It was established that increasing the distances d_1 and d_2 will enhance the steric hindrance in the 'fjord-region' of the molecule resulting in a higher Gibbs energy of activation for the helix inversion. Accordingly, larger moieties X and Y show slower thermal rotary steps in these motors.[7]

In order to speed up the rotation process by releasing some of the steric hindrance, four new molecules **2–5** with a tetrahydronaphthalene moiety in the upper part and different bridging units in the lower part, were designed (Fig. 1). All alkenes **2–5** have a symmetric lower part and can adopt a stable (Me_{ax}) and less-stable (Me_{eq}) form (Fig. 1). As a consequence, photoisomerisation to yield the less-stable forms (**2b–5b**) is expected to be followed by thermal isomerisation to revert to the original stable isomers (**2a–5a**). We realised that the removal of one arene ring in the upper part (**1a** *vs.* **5a**; **1b** *vs.* **2a**) does not only strongly reduce steric interaction at the 'fjord-region' during rotary motion (helix inversion step) but allows a competing *cis*-stilbene photocyclisation pathway to take place.



1a: X = CH_2, Y = CHCH
1b: X = CH_2, Y = S

2a: Y = S
3a: Y = $C(CH_3)_2$
4a: Y = CH_2CH_2
5a: Y = CHCH

2b: Y = S
3b: Y = $C(CH_3)_2$
4b: Y = CH_2CH_2
5b: Y = CHCH

Fig. 1 Second generation of light-driven molecular motors (one enantiomer drawn) with phenanthrene (**1**) and with naphthalene (**2–5**).

The helical-shaped molecules were synthesised in an identical manner as the second generation of molecular motors,[7] using diazo-thioketone coupling to introduce the central double bond, and were fully characterized by ^1H, ^{13}C, COSY and NOESY NMR and high resolution mass spectroscopy.† ^1H NMR studies of **2a–5a** revealed that the methyl substituents in the upper part adopt a pseudo-axial orientation. This was concluded from coupling constants in the range of 4.0–6.6 Hz for the proton H2′ at the stereogenic centre indicating an equatorial orientation, which was confirmed by X-ray analysis of olefin **5a** (Fig. 2).

The second generation molecular motor with the lowest Gibbs energy of activation at room temperature ($\Delta^{\ddagger}G^{\theta}$ = 91.6 kJ mol^{-1}, X = CH_2, Y = S, **1b**, Fig. 1) found so far,[7] showed its thermal conversion at room temperature with a half-life of approximately 40 min. Since the steric hindrance in the new olefins **2–5** was expected to be considerably reduced with respect to the motor molecule with a tetrahydrophenanthrene upper part, even faster thermal conversions of less-stable olefins **2b–5b** at room temperature were expected. Therefore, irradiation was performed at −40 °C to be able to monitor formation of the less-stable isomers **2b–5b**. Initially, the photochemical conversions were followed by UV spectroscopy and spectra were taken at regular time intervals until no change occurred anymore. However, the products of irradiated samples (313 nm, Hg-lamp) of olefins **2–4** could not be reverted to the original olefins. Even when these samples were heated as high as 60 °C for 18 h, no reversal to the starting compounds could be observed, which led to the conclusion that an irreversible reaction took place. Only olefin **5** showed reversible behavior, as heating of an irradiated sample at 60 °C for 18 h resulted in stable **5a** exclusively. To characterise the products of the photochemical experiments, irradiation was repeated at higher concentrations in toluene-d_8 or benzene-d_6 at room temperature.

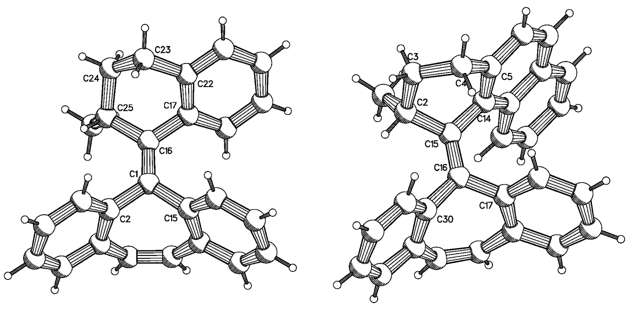


Fig. 2 PLUTO drawings of olefins **1a** and **5a**.

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† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b2/b208323j/

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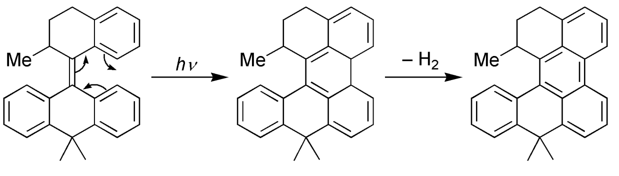
Irradiation of olefin **2a** gave an undefined black precipitate and no further attempts were undertaken to characterize this product. A very slow conversion was observed upon irradiation of olefin **4a**. As formation of an irreversible product was observed during the initial UV experiments and due to low conversion the characterisation of the product was not pursued. In the case of olefin **3a** a fast and very clean conversion to a single product **7** was observed. Photocyclisation occurred presumably resulting in the formation of intermediate **6**, which, after loss of hydrogen gave ring closed product **7**, as was supported by ^{1}H NMR and high resolution mass spectroscopy analysis. This sequence of events was foreseen to be a possible, but undesirable, side process (Scheme 1).



3a **6** **7**

Scheme 1 Photocyclisation of olefin **3a**.

On the contrary irradiation of stable olefin **5a** gave a clean photochemical conversion to less-stable isomer **5b** exclusively, showing a 32:68 ratio at the photostationary state (Table 1). Formation of cyclised or other side products was not observed.

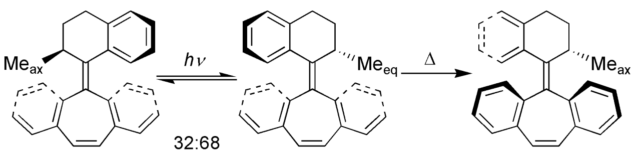
Table 1 Conditions[a] and results of irradiation experiments

Olefin	Conc./M	Solvent	Time/h	Product
2a	9.8×10^{-3}	Toluene-d_8	21	Unidentified product
3a	9.5×10^{-3}	Benzene-d_6	21	53% **7**
4a	9.1×10^{-3}	Benzene-d_6	21	95% **4a**
5a	1.0×10^{-2}	Benzene-d_6	11	32:68[b]

[a] Irradiation experiments were carried out using an Hg-lamp with Pyrex filter at room temperature. [b] Ratio of **5a** *vs.* **5b** at photostationary state.

NMR studies revealed that the H2′-proton showed an upfield shift from 3.34 to 2.68 ppm. Coupling constants of 5.9 and 11.8 Hz were found for H2′ which demonstrates that the adjacent methyl substituent indeed adopts the energetically unfavorable equatorial orientation in **5b**. Heating the mixture of stable **5a** and less-stable **5b** resulted in a quantitative conversion to stable isomer **5a** (Scheme 2). This result confirms that the photochemical conversion is an energetically uphill process and that the subsequent thermal conversion is energetically downhill as observed before with motors **1**. The rate of the thermal conversion was determined at four different temperatures over the range of 40 to 70 °C. The conversions were monitored by ^{1}H NMR recorded at regular time intervals and the integration of the two different methyl substituents were used to determine the ratio between both isomers. The rate constants (k) lead to the activation parameters $E_a = 94.4 \pm 3.8$ kJ mol^{-1}, $\Delta H^{\ddagger} = 91.7 \pm 3.7$ kJ mol^{-1}, $\Delta S^{\ddagger} = -51 \pm 11$ J K^{-1} mol^{-1}, $\Delta^{\ddagger}G^{\theta}$ (20 °C) = 106.6 ± 0.4 kJ mol^{-1}, k^{θ} (20 °C) = $(6.13 \pm 0.97) \times 10^{-7}$ s^{-1}, $t_{1/2}{}^{\theta}$ (20 °C) = 314 ± 50 h.

A remarkable high Gibbs energy of activation at room temperature ($\Delta^{\ddagger}G^{\theta}$ (20 °C) = 106.6 ± 0.4 kJ mol^{-1}) was found for the thermal conversion of less-stable **5b** into stable **5a**. When compared to its tetraphenanthrene substituted analogue **1a** (Fig. 1, $\Delta^{\ddagger}G^{\theta}$ (20 °C) = 102.6 ± 0.2 kJ mol^{-1}), an increase of the Gibbs energy of activation at room temperature of 4.0 kJ mol^{-1} was found. The half life time at room temperature ($t_{1/2}{}^{\theta}$) of less-stable **5b** of 314 h is more than five times longer than the half life time of tetrahydrophenanthrene substituted motor **1a** ($t_{1/2}{}^{\theta}$ (20 °C) = 60.1 ± 5.3 h). At first glance this is a surprising result since the tetrahydrophenanthrene substituted motor **1** is sterically more demanding in the 'fjord-region' compared to motor **5** with the smaller tetrahydronaphthalene upper part. Apparently, the encountered steric repulsion during the thermal conversion is not the sole parameter governing the height of the Gibbs energy of activation.



stable **5a** *less-stable* **5b** *stable* **5a**

Scheme 2 Rotation behavior of motor **5**.

Table 2 Relevant torsion angles of cyclohexene ring of motor **1a** and **5a**

Motor **1** Carbon atoms	Angle/°	Motor **5a** Carbon atoms	Angle/°
16–15–14–5	−119.55	1–16–17–22	−136.16
16–15–2–3	−121.02	1–16–25–24	−203.61
15–14–5–4	1.13	16–17–22–23	−7.21
15–2–3–4	2.36	16–25–24–23	28.70

In order to find additional factors affecting the thermal step, a comparison of X-ray structures of stable motors **1a** and **5a**,[8] which only differ in the annelated ring, is particularly revealing. The relevant torsion angles outlined in Table 2, indicate that the shape of the dibenzoheptenyl lower parts of both motors **1** and **5** do not differ significantly. In the upper part of motors **1a** and **5a**, considerable conformational differences were found. The dihedral angles of the cyclohexene ring of **1a** indicate that it adopts a boat conformation. On the other hand, the dihedral angles of the cyclohexene ring of **5a** show that it is strongly resembling a twisted boat conformation. Apparently, the more severe steric hindrance in the fjord region of motor **1a** forces its cyclohexene ring to an energetically unfavorable boat conformation, whereas the lower steric hindrance in motor **5a** results in more conformational flexibility in the cyclohexene ring, allowing it to adopt an energetically favorable twisted boat conformation. Preliminary molecular mechanics calculations show that for the unstable form of **1a** and **5b** (Me$_{eq}$) the same conformational differences exists. These results strongly indicate that, in addition to steric hindrance during helix inversion (thermal isomerisation), differences in Gibbs energies of ground states (ΔG^{θ}) of stable and unstable forms are of such magnitude that they become a crucial parameter in the control of speed of rotation of these unidirectional rotary motors.

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8 *Crystal data* for **5a**, $C_{26}H_{22}$, $M_r = 334.46$, monoclinic, $P2_1/c$, $a = 7.4391(4)$, $b = 26.165(2)$, $c = 9.2788(6)$ Å, $\beta = 92.125(1)°$, $V = 1804.8(2)$ Å^3, $Z = 4$, $D_c = 1.231$ g cm^{-3}, λ(Mo-K$\bar{\alpha}$) = 0.71073 Å, $\mu = 0.69$ cm^{-1}, $F(000) = 712$, $T = 90$ K, GooF = 1.032, $wR(F^2) = 0.1098$ for 3449 reflections with $F_o \geqslant 4.0\sigma(F_o)$ criterion of observability. CCDC 192274. See http://www.rsc.org/suppdata/cc/b2/b208323j/ for crystallographic data in CIF or other electronic format.