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 machines1 has stimulated chemists to construct mechanical molecular systems including switches,2 motors,3 shuttles4 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. The key features of these second generation molecular motors, 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 which 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 photoisomerization 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 d1 and d2 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 (Meax) and less-stable (Meaq) 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.

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, 13C, 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 (∆G° = 91.6 kJ mol−1, X = CH2, 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-d8 or benzene-d6 at room temperature.

† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b2/b208323/
Irradiation of olefin 2a gave an undefined black precipitate and no further attempts were undertaken to characterise 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 $^{1} \text{H}$ NMR and high resolution mass spectroscopy analysis. This sequence of events was foreseen to be a possible, but undesirable, side process (Scheme 1).

![Scheme 1 Photocyclisation of olefin 3a.](image)

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>
<thead>
<tr>
<th>Olefin</th>
<th>Conc./M</th>
<th>Solvent</th>
<th>Time/h</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>$9.8 \times 10^{-3}$</td>
<td>Toluene-$d_{8}$</td>
<td>21</td>
<td>Unidentified product</td>
</tr>
<tr>
<td>3a</td>
<td>$9.5 \times 10^{-3}$</td>
<td>Benzene-$d_{6}$</td>
<td>21</td>
<td>53% 7</td>
</tr>
<tr>
<td>4a</td>
<td>$9.1 \times 10^{-3}$</td>
<td>Benzene-$d_{6}$</td>
<td>21</td>
<td>95% 4a</td>
</tr>
<tr>
<td>5a</td>
<td>$1.0 \times 10^{-3}$</td>
<td>11</td>
<td>32:68</td>
<td></td>
</tr>
</tbody>
</table>

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

NMR studies revealed that the H$_2$-proton showed an upfield shift from 3.34 to 2.68 ppm. Coupling constants of 5.9 and 11.8 Hz showed a 32a. Comparison of X-ray structures of stable motors 1a and 5a, which only differ in the annelated ring, is particularly revealing. The relevant torsion angles outlined in Table 2, indicate that the statica and dynamica of the dibenzoheptyl 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 ($M_{eq}$) 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 ($\Delta G^{o}$) of stable and unstable forms are of such magnitude that they become a crucial parameter in the control of speed of rotation of this unidirectional rotary motors. Financial support from the Netherlands Foundation for Scientific Research (NWO-CW) is gratefully acknowledged.

Notes and references

8. Crystal data for 5a, C$_{29}$H$_{32}$, M$_{r}$ = 334.46, monoclinic, P2$_{1}$/c, a = 7.2149(4), b = 26.165(2), c = 9.2988(6), $\beta$ = 92.125(1)°, V = 1804.8(2), $\mathbf{A}$ = 1.231 g cm$^{-3}$, $\Delta$(Mo-K$_{\alpha}$) = 0.71073 A, $\lambda$ = 0.69 cm$^{-1}$, F(000) = 712, T = 90 K, Goof = 1.032, wR(F$^{2}$) = 0.0198 for 3490 reflections with $F_{o} > 4.00 F_{c}$ criterion of observability. CCDC 192274. See http://www.rsc.org/suppdata/cc/b2/b208323j for crystallographic data in CIP or other electronic format.