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Controlling the speed of rotation in molecular motors. Dramatic acceleration of the rotary motion by structural modification†

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Substitution of a 6-membered by a 5-membered ring upper half in the light driven second generation molecular motors resulted in a dramatic increase of the speed of rotation.

The study of synthetic motors on the molecular scale is one of the most challenging topics at the intersection of chemistry, physics and biology. Synthetic approaches towards artificial machinery have resulted in several elegant molecular devices in which controlled motion at the molecular level is the key feature, including switches, brakes, gears, turnstiles, shuttles, scissors, elevators, rotating modules and muscles. Since the development of the first light driven molecular motor 1 (Fig. 1), based on symmetric biphenanthrylidenes, several modifications have been made in order to increase the speed of rotation necessary for application. In this motor repetitive unidirectional rotation around the central double bond (the axis of rotation) is achieved by two photochemical olefin isomerisations, each followed by a thermal conversion, resulting in a four step 360° rotation cycle. 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 molecule in its more stable form (axial orientation of the methyl substituent), a photoisomerisation takes place resulting in a helix inversion, whereas the methyl substituent adopts the less stable equatorial conformation. In order to isomerise to the more stable form, the naphthalene upper part must slip past the lower part of the molecule, resulting in a helix inversion. For the second generation light driven molecular motors, it was established that an increase of the size of atoms X and Y enhances the steric hindrance in the ‘fjord region’ of the molecule (Fig. 1), resulting in a higher Gibbs free energy of activation for the helix inversion and, accordingly, larger moieties X and Y show slower thermal rotary steps in these motors. Several unsuccessful attempts to enhance the speed of rotation were made by substitution of the naphthyl in 2 for a phenyl moiety or displacement of the methyl substituent out of the ‘fjord region’. Molecular motor 3 (Fig. 1) in which the 6-membered rings present in 1 were replaced by 5-membered rings, shows an increase in the speed of rotation due to the considerable reduction of the steric hindrance in the ‘fjord region’. This 5-membered overcrowded alkene represents the fastest light driven molecular motor reported so far.

In order to accelerate further the rotation process by reduction of steric hindrance, a new second generation molecular motor 5 with a 5-membered upper half ring and a fluorene lower half was designed (Fig. 2) and its dynamic behaviour was compared with the first generation analogue 3 and the second generation motors with a 6-membered upper half 4.

The helical overcrowded alkenes 4 and 5 were synthesised using a Staudinger type diazo-thioketone coupling to generate the double bond and were characterised fully by 1H and 13C NMR and HRMS. Chemical shifts in the 1H NMR for the methyl substituents in the upper half at high field, 1.40 and 1.25 ppm for 4 and 5 respectively, are consistent with a pseudoaxial orientation, a preferred conformation which was confirmed by the X-ray structure of compound 5 (Fig. 3). It was established that the (S)-enantiomer showed a preferred (M)-helicity, while the (R)-enantiomer showed a preferred (P)-helicity.

Irradiation experiments (366 nm, Hg-lamp) were performed at −10 °C in hexane or dodecane. The formation of the less stable isomer by cis–trans isomerisation (Scheme 1) was observed by UV–Vis as a shift of the absorption at 390 nm to a broader band at 420 nm (Fig. 4). Subsequent thermal isomerisation by heating of the samples to rt for the 5-membered alkene 5 or to 100 °C for the 6-membered alkene 4 resulted in identical UV–Vis spectra to those of the initial states.

Irradiation of NMR samples (366 nm, Hg-lamp) was performed at −40 °C to characterise the unstable intermediates. Upon

Fig. 1

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† Electronic Supplementary Information (ESI) available: Detailed experimental procedures for the synthesis of alkenes 4, 5a and 5b. See http://dx.doi.org/10.1039/b507264f

Fig. 2 New second generation molecular motors (R enantiomer shown).
irradiation of a toluene-D₈ solution of alkene 5 a downfield shift of the doublet corresponding to the methyl substituent at 1.21 ppm to 1.46 ppm was observed indicating a pseudoaxial to pseudoequatorial conformational change (Scheme 1). A photostationary state (PSS) of 75 : 25 (unstable : stable) was determined by integration of the doublet signal. Warming the irradiated sample to rt resulted in a first order isomerisation process to give stable 5 with a pseudoaxial orientation of the methyl substituent (Scheme 1).

Irradiation of the 6-membered alkene 4 was carried out at rt, again showing a downfield shift of the methyl signal (1.08 to 1.22 ppm) with an unstable : stable ratio 91 : 9 in the PSS. Thermal isomerisation of the unstable form of 4 to its stable isomer required heating to 100 °C overnight.

Given the helical structure of the olefins 4 and 5 the photochemical and thermal isomerisations can also be monitored by CD spectroscopy (Fig. 5). Enantiomer resolution of 4 and 5 was achieved by chiral HPLC (Chiracel-OD column). Irradiation of the enantiopure motor molecules at low temperature shown complete inversion of the CD signal, indicating photoisomerisation and simultaneous helix inversion. Heating the samples to rt for the 5-membered alkene 5 or to 100 °C for the 6-membered alkene 4 fully restored the CD spectra of the initial states.

After irradiation of the motor molecules 4 and 5, the samples were heated and the change in the intensity of the CD bands over time were measured at several temperatures. This allowed monitoring of the rate of conversion of the less stable isomers and, therefore, a rate constant (k) at different temperatures was obtained, corresponding to a first order kinetic process. Applying the Eyring plot for different temperatures allows the calculation of the enthalpy of activation (ΔHº) and entropy of activation (ΔSº) and eventually the Gibbs free energy of activation (ΔGº), the rate constant at (k₀) and half life at rt (t₁/₂) can be determined. The results are summarised in Table 1, together with the values determined for the two different thermal steps of the symmetric 5-membered ring molecular motor 3.

Comparison of the half lives of the new motor 5 with the first generation 5-membered motor 3 shows that although the trans-unstable (obtained from cis-3) to trans-stable thermal step is faster for 3, the second cis-unstable (obtained from trans-3) to cis-stable thermal step necessary to complete the 360° cycle is slower. The most remarkable finding is that the change of a 6-membered ring for a 5-membered ring upper half (4 → 5) increases the speed of rotation by a factor of approx. 10⁸ times. It should be emphasised that the half life of the unstable form of the 6-membered ring alkene 4 is the longest reported, while the 5-membered alkene 5 is the fastest one in completing the full 360° cycle.

To prove unequivocally the unidirectionality of the rotary process by ¹H NMR, pure cis-alkene 6, with a non-symmetrical fluorene lower half, was synthesised (see ESI†). Irradiation

![Scheme 1 Photochemical isomerisation and thermal helix inversion.](image)

![Fig. 3 Pluto drawing for (R)-5.](image)

![Fig. 4 UV–Vis spectra in hexane of 5 before (black) and after irradiation (grey).](image)

![Fig. 5 CD spectra in hexane of 5 before (black) and after irradiation (grey).](image)

![Table 1 Isomerisation parameters for 3, 4, and 5](image)
(366 nm, Hg-lamp) at −40 °C of a toluene-d₈ solution of stable cis-alkene 6 afforded a PSS comprising trans-unstable/cis-stable with a ratio 77/23 (Scheme 2), determined by integration of the methoxy singlets, since the ratio cis-stable : trans-stable is equivalent to the ratio cis-stable : trans-unstable at the PSS). Thermal cis→trans isomerisation was excluded, which confirms the unidirectionality of the thermal irreversible isomerisation. Similar results were obtained when a second irradiation of the resulting cis-stable→trans-stable mixture was carried out at −40 °C. The ratio trans-unstable : cis-stable at the PSS is known from the previous irradiation experiment and the ratio cis-unstable : trans-stable can be calculated from the integration of the doublet signals for the pseudoaxial and pseudoequatorial methyl substituents. Heating of the irradiated sample to complete the 360° cycle showed in this case transformation of cis-unstable exclusively to cis-stable, demonstrating the unidirectionality of the overall 360° rotary cycle.

It should be noted that fast rotation is observed in spite of using a fluorene lower half in motor 5, which due to the rigid planar structure does not allow bending and therefore makes difficult for the upper naphthalene unit to pass along the lower half. It is envisaged that the use of more flexible lower halves might increase the speed of rotation even further. The new light driven molecular motor described here is not only the fastest, but also the smallest reported so far.

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Notes and references
17 Chemical formula: C₂₇H₂₀; M. 344.46 g mol⁻¹; unit cell dimensions a = 32.404(2) Å, b = 8.9496(4) Å, c = 8.9496(4) Å, V = 8138.3(8) Å³; T 100(1) K; trigonal R3; Z = 8; μ (M o Kα), cm⁻¹ = 0.71073 Å⁻¹; wR(F) = 0.1029 for 3991 reflections with Fo ≥ 0 and R(F) = 0.0412 for 3399 reflections with Fo ≥ 4σ(Fo) and 324 parameters. CCDC 272911. See http://dx.doi.org/10.1039/b507264f for crystallographic data in CIF or other electronic format.