On the effect of donor and acceptor substituents on the behaviour of light-driven rotary molecular motors

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Light-driven rotary molecular motors based on overcrowded alkenes can be substituted with electron-donating and electron-withdrawing substituents (R = OMe, Cl and CN) in direct conjugation with the central double bond (the axis of rotation) without having a significant influence on the rate-limiting, thermal isomerisation step of their rotary cycle. This indicates that in this system, it is predominantly steric factors that determine the barrier to the thermal helix inversion. In contrast, the quantum yield and photoequilibria in the photochemical step were found to be quite sensitive to the combination of substituent and solvent employed.

Introduction

In recent years, extensive research on biological motors has shown how nature elegantly controls motion at the molecular scale in a variety of cellular processes, including ion and proton pumping, cellular translocation, and ATP synthesis.[1] The development of robust synthetic systems that are capable of mimicking the rotary action of biological motors is a major contemporary challenge because it could allow chemists to control motion at the molecular level.[2] Successful designs for synthetic rotary molecular motors have been reported, including those powered by light,[3–6] and chemical energy.[7–9]

One of the most promising designs of a rotary molecular motor is based on chiral overcrowded alkenes, exemplified by structure **1** (Fig. 1).[4a] The repetitive unidirectional rotation of the upper-half relative to the lower-half in these 'second generation' light-driven molecular motors is achieved by two energetically uphill photochemical alkene isomerisations, each followed by a rate-limiting, thermodynamically downhill thermal isomerisation (*vide infra*, Fig. 2). The unidirectionality is governed by the configuration at the stereogenic center.

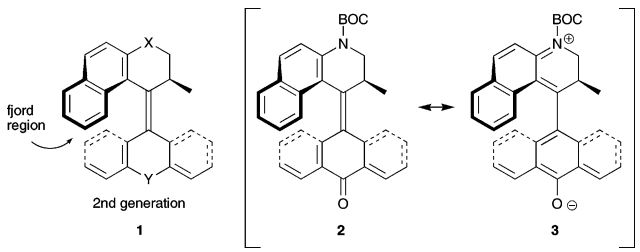

Fig. 1 Examples of 2nd-generation light-driven molecular motors.

One of the major challenges to harnessing work from these systems is making the rotation fast enough to compete with Brownian motion.[2a,c] The necessity of the task is illustrated by a comparison of the first version of the 'second-generation' molecular motor **1** (X = Y = S), with the bacterial flagellar motor of *Vibrio alginolyticus.* At rt, **1** required 400 h to complete a single rotation, whereas the flagellar motor is capable of speeds up to 1000 rotations per second.[10]

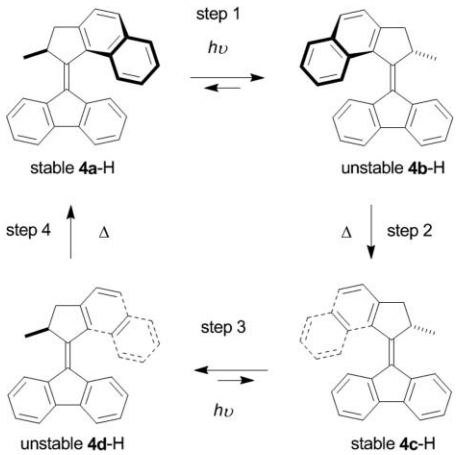

Fig. 2 Rotary cycle of molecular motor with a lower-half derived from fluorenone.

Recently, a number of changes to the original design have been made to develop motors with a much faster rotary cycle.[11–15] In one approach, it was found that exchanging the bridging moieties X and Y in **1** (Fig. 1) to smaller groups (S→O or CR_2), led to a 300-fold drop in the barrier to thermal helix inversion.[4a] In these studies, however, several molecules did not fit the trend expected if the acceleration was derived exclusively from a reduction of steric hindrance in the fjord region. This raises the question: what is the origin of the rate acceleration—is it strictly steric/conformational, or do electronic factors also contribute?

The subsequent discovery that **2** (Fig. 1) had a barrier to thermal helix inversion which was much lower than **1** implicated the contribution of a "push–pull" resonance effect.[16–19] In this rationale, the elongation of the central alkene mediated by a greater contribution from the resonance structure **3**, led to a reduction in

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the steric interactions that prevent thermal helix inversion (similar to a vinylogous amide).

Here we show that in the 'second generation' design of molecular motor (**1**, X = Y = '–'), containing a fluorenyl 'lower-half', the presence of electron-donating or withdrawing substituents in the upper-half positioned in direct conjugation with the central olefin exerts no significant influence on the rate-determining thermal helix inversion. In this system, the fluorenyl lower-half was chosen because of the possibility that it could act as an electron acceptor by virtue of the aromatic character of the fluorenyl anion, as well as the relative ease of preparation of these functionalised alkenes.

Results and discussion

Molecular design

The systems investigated in this study are based on the second-generation motor (±)-**4**-H (Fig. 2).[20] In the more stable isomer (stable **4a**-H), the methyl substituent adopts an axial orientation to prevent steric hindrance. In the photochemical steps 1 and 3, a light-mediated isomerisation of the central double bond forces the methyl substituent to adopt an equatorial orientation, hence forming the less-stable isomer **4b**-H. In the thermal steps 2 and 4 that follow, the molecule isomerises back to the thermodynamically preferred orientation in which the methyl group re-adopts an axial conformation. During this step, the naphthalene upper part passes along the lower part of the molecule leading to simultaneous helix inversion to give **4c**-H. If the molecule is irradiated continuously, these steps continue in succession, resulting in the continuous unidirectional rotation of the upper-half relative to the lower-half.

To evaluate what influence this proposed resonance contribution would have on the motors' behaviour, a series of molecular motors was needed, in which each molecule was functionalised with electron-donating or electron-withdrawing substituents. Parent structure **4**-R (where R = H, Fig. 3) seemed to be a suitable candidate because the substituent 'R' at the 4-position of the naphthalene ring is placed in direct conjugation with the central alkene. Importantly, it should exert no direct effect on the steric crowding in the fjord region or on the conformational chemistry of the overcrowded olefin.

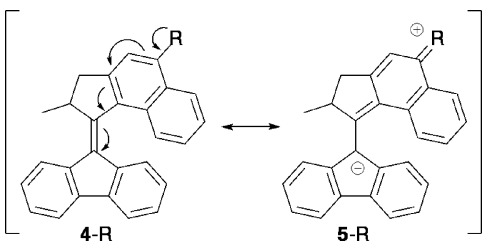


Fig. 3 Possible elongation of the central olefin due to stabilisation of the zwitterionic resonance form.

It was envisioned that if the lower-half is derived from the relatively acidic fluorenyl group (pK_a ~22.8), it could stabilise the resonance form possessing a negative charge at the olefinic atom (as in **5**-R, Fig. 3). The fluorenyl anion moiety should be stabilised by its aromatic character. In this way, the presence of electron-donating groups as R should also enhance the contribution of the zwitterionic resonance structure **5**-R, whereas the presence of electron-withdrawing groups as R should minimise it. If the presence of donating *vs.* withdrawing groups has a significant effect on the nature of the double bond in the unstable form, it should result in elongation of the central alkene, which could in turn reduce steric crowding in the fjord region and lower the thermal barrier to helix inversion.

Synthesis

Second-generation rotary molecular motors derived from overcrowded alkenes are typically prepared by a Staudinger diazo–thioketone coupling, which allows a gradual introduction of the steric hindrance in the olefin. It was initially envisioned that the appropriately functionalised motors could be prepared from the thioketone of the lower-half and the upper-half possessing a diazo function (R^1 = S, R^2 = N_2, Fig. 4).

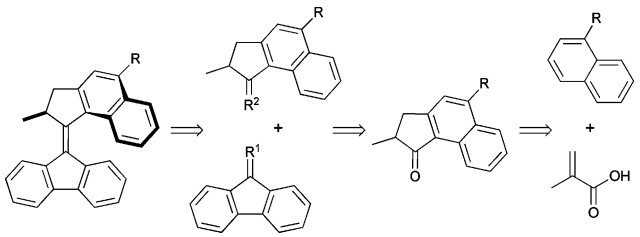
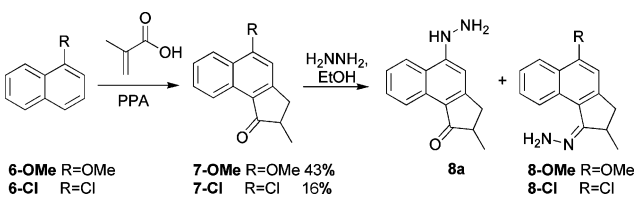


Fig. 4 Retrosynthetic analysis of substituted molecular motors.

We anticipated that the required series of substituted benzoindanones could be made from the corresponding substituted naphthalene and methacrylic acid in PPA in a one pot tandem Friedel–Crafts acylation–Nazarov cyclisation sequence.[21] While this one-pot preparation works acceptably on only *ortho*/*para* directing substituents, we believed that electron-withdrawing groups could be introduced after the core structure of the ketone was complete.

The synthesis of ketones decorated with a methoxy (EDG) and a chloride were pursued initially (Scheme 1). 1-Methoxynaphthalene **6**-OMe and 1-chloronaphthalene **6**-Cl were treated with methacrylic acid in PPA at 110 °C to give the desired ketones **7**-OMe and **7**-Cl, respectively. While the yields are modest, this one-pot procedure provides access to the desired ketones in one step from commercial material, unlike any other route which we could envision. Unfortunately, treatment of 1-bromonaphthalene with similar conditions at the same or at higher temperatures led to complex mixtures and very low yields (>2%) of product.



Scheme 1 Synthesis of substituted benzoindanones and unexpected nucleophilic aromatic substitution by hydrazine.

Treatment of ketone **7**-OMe with hydrazine hydrate in refluxing ethanol lead to the formation of a mixture of hydrazine **8a** and the desired hydrazone **8**-OMe (Scheme 1). Presumably, **8a** is formed

via a S_NAr pathway. Treatment of **7**-Cl under identical conditions also lead to a complex mixture of **8a**, **8**-Cl, and the hydrazone of **8a**. Reducing the temperature did not improve the selectivity significantly. This surprising reactivity may be facilitated by the fact that the rate-limiting addition of the nucleophile (here hydrazine) to the 1-position of the naphthalene ring disrupts the aromaticity less than would be the case on a similarly substituted phenyl. This, in combination with the leaving group methoxide or chloride being positioned *para* to the electron-withdrawing ketone function, likely activates these compounds toward S_NAr reactions.

To circumvent this undesired reactivity, we explored the possibility of coupling the thioketone of the upper-half with diazofluorenone (Fig. 4, $R^1 = N_2$, $R^2 = S$).[22] Methoxy-substituted ketone **7**-OMe was treated with P_2S_5 in benzene at reflux for 2 h to give the desired thioketone **9**-OMe in good yield. The stability of this thioketone is remarkable given that it possesses a proton 'α' to the thioketone function, and can tautomerise to the thioenol. **9**-OMe can be purified by SiO_2 gel chromatography and stored for at least 3 months at rt without detectable degradation. The stability of this thioketone is also highlighted by its low reactivity: treatment of **9**-OMe with diazofluorenone[23] in benzene at rt gave no reaction. However, heating **9**-OMe with diazofluorenone to reflux for 2 h surprisingly gave alkene **4**-OMe directly in 71% yield, with no detectable episulfide **10**-OMe.[24] Spontaneous desulfurisation of thioepoxides to the corresponding olefins has been observed by Harpp and Warren[25] during their synthesis of fluorenyl olefins, though it is somewhat surprising that it occurs in the formation of overcrowded alkenes as well. Bifluorenylidene was also formed as a byproduct in this reaction, and proved difficult to separate from the desired product **4**-OMe.

The preparation of **4**-Cl by the analogous route was more challenging because thioketone **9**-Cl is considerably less stable than **9**-OMe. Treatment of ketone **7**-Cl with P_2S_5 in benzene for 2 h gave thioketone **9**-Cl as a mixture contaminated with the corresponding thioenol (approx. 2 : 1) as well as small amounts of unidentified impurities. These conditions maximised conversion while minimising side reactions including the tautomerisation to the thioenol. Tautomerisation occurred to some extent under all conditions tested, including during purification on silica gel, and upon standing at rt over the course of hours. The optimal procedure we found was the immediate filtration of the crude product containing **9**-Cl over a plug of silica, followed by treatment of the crude product with diazofluorenone to give a mixture of the episulfide **10**-Cl and alkene **4**-Cl (the ratio depended on the reaction time, likely because of spontaneous desulfurisation occurring to some extent). This mixture was treated directly with Ph_3P in refluxing toluene for 12 h to effect the reductive desulfurisation of the episulfide to give **4**-Cl in 30% yield from **7**-Cl.

With unsubstituted motor **4**-H, **4**-OMe (with an EDG), and **4**-Cl (with a weak EWG) in hand, we anticipated that it would be instructive to examine the effect of a strongly electron-withdrawing group also. For this purpose, we chose the cyano group since it is very electron-withdrawing, while it is not expected to exert a dramatic effect on the photoisomerisation step (for this reason, electron-withdrawing substituents which could independently influence excited state processes such as nitro or keto groups were avoided).[26–28]

In an initial attempt to prepare alkene **4**-CN *via* a synthetic route analogous to that just described for **4**-Cl, **7**-Cl was transformed to **7**-CN in 78% yield using the palladium catalyzed cyanation conditions described by Confalone and Jin[29] (Scheme 2). Unfortunately, attempts to prepare the nitrile substituted compound **4**-CN *via* thioketone **7**-CN were unsuccessful since the ketone **7**-CN was found to be relatively unreactive to P_2S_5 and Lawesson's reagent. Longer reaction times or higher temperatures (>140 °C) resulted in slow degradation of the ketone. Fortunately, we found that by increasing the reaction temperature of the palladium catalyzed cyanation procedure from 120 °C to 150 °C we were able to transform aryl-chloride **4**-Cl into the nitrile functionalised motor **4**-CN in 90% yield.

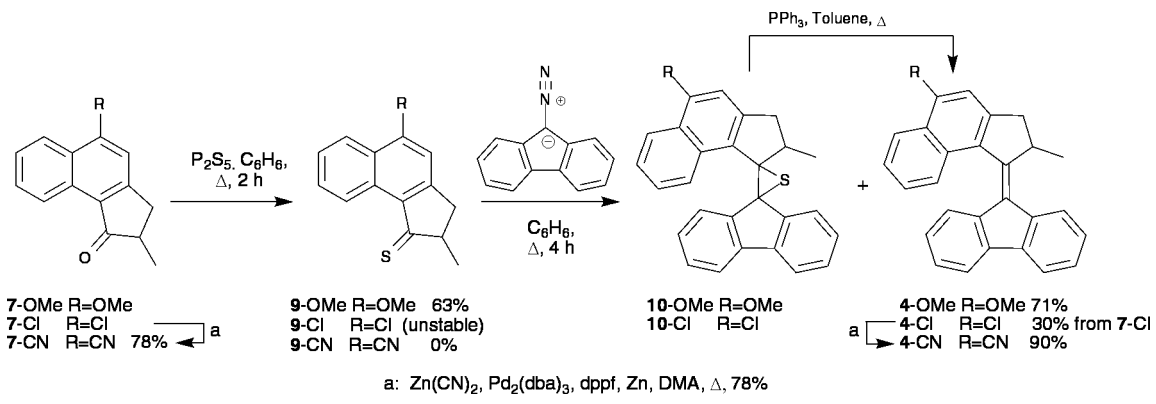
UV–vis spectra

Comparison of the UV–vis spectra of **4**-OMe, **4**-Cl, and **4**-CN with that of the parent motor **4**-H shows that the introduction of both electron-donating and electron-withdrawing groups leads to a modest red-shift of the longer wavelength absorption attributed to the central olefin (Fig. 5).[30,31]

Analysis of the rotary cycle

Step 1: Photochemical isomerisation

The photochemical isomerisation was studied initially by UV–vis spectroscopy at −20 °C. Based on the known half-life of **4**-H at rt (4.3 min), it was anticipated that the thermal isomerisation of



Scheme 2 Synthesis of substituted molecular motor molecules **4**-OMe, **4**-Cl, and **4**-CN.

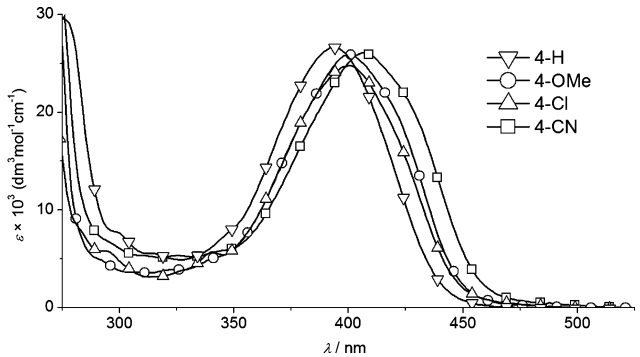


Fig. 5 UV–vis spectra of **4**-H (▽), **4**-Cl (△), **4**-OMe (○), and **4**-CN (□) in hexane at 20 °C.

the unstable isomers of the new alkenes would be negligible at this temperature. In analogy with the behaviour observed for **4**-H, irradiation ($\lambda = 365$ nm) of racemic[32] **4**-OMe, **4**-Cl and **4**-CN in hexane at −20 °C to their photostationary states (PSS) resulted in a red shift of the major absorption band of each compound (Fig. 6). This change is consistent with the formation of the unstable isomers of **4**-OMe, **4**-Cl and **4**-CN. During the irradiation of each compound, clear isosbestic points were visible, indicating that the photoisomerisation was a clean, unimolecular process.

When the photoirradiation was repeated using CH_2Cl_2 as the solvent, **4**-Cl and **4**-CN gave the expected red-shift of the long wavelength absorption band. However, photoirradiation of **4**-OMe under identical conditions gave only a small photoconversion, even after extended irradiation times. This solvent and substrate dependent behaviour is reminiscent of similar observations made in the literature concerning the photoisomerisation of related chromophores bearing donor and acceptor substituents across the central double bond including stilbenes and azobenzenes substituted with a nitro group.[26b,33–39] In a detailed study, Görner and Gruen observed a dramatic reduction in the PSS photoconversion of *trans*-4-nitro-4′-dimethylaminostilbene to the *cis* isomer when polar solvents were used instead of apolar ones.[33] King and coworkers[34] also observed a similar trend in photoisomerisation quantum yields for donor–acceptor imines, stilbenes and azobenzenes. Additionally, Diederich and coworkers[36] observed a dramatic reduction in the quantum yields of trans→cis isomerisation of donor–acceptor 1,2-diethynylethenes upon changing the solvent from hydrocarbon solvents to more polar solvents such as $CHCl_3$, as well as DMF and MeCN. In contrast to **4**-OMe, the nitro group is a common feature of systems that exhibit a strongly solvent-dependent photoequilibrium. In the case of the nitro-stilbene derivatives, the intermediacy of a charge-separated state in the photoisomerisation was implicated in this solvent dependence. Thus, the origin of the solvent dependence of the photoequilibrium **4**-OMe is unclear at present.

Low temperature ^{1}H NMR analysis of the stable/unstable isomers

Irradiation of the four motors[32] at 365 nm in toluene-d_8 at −40 °C allowed the characterisation of the unstable isomers as well as the determination of the PSS by ^{1}H NMR spectroscopy. The ^{1}H NMR spectra of the PSS mixtures indicate that in all cases the absorptions of the methyl substituent at the stereogenic center of

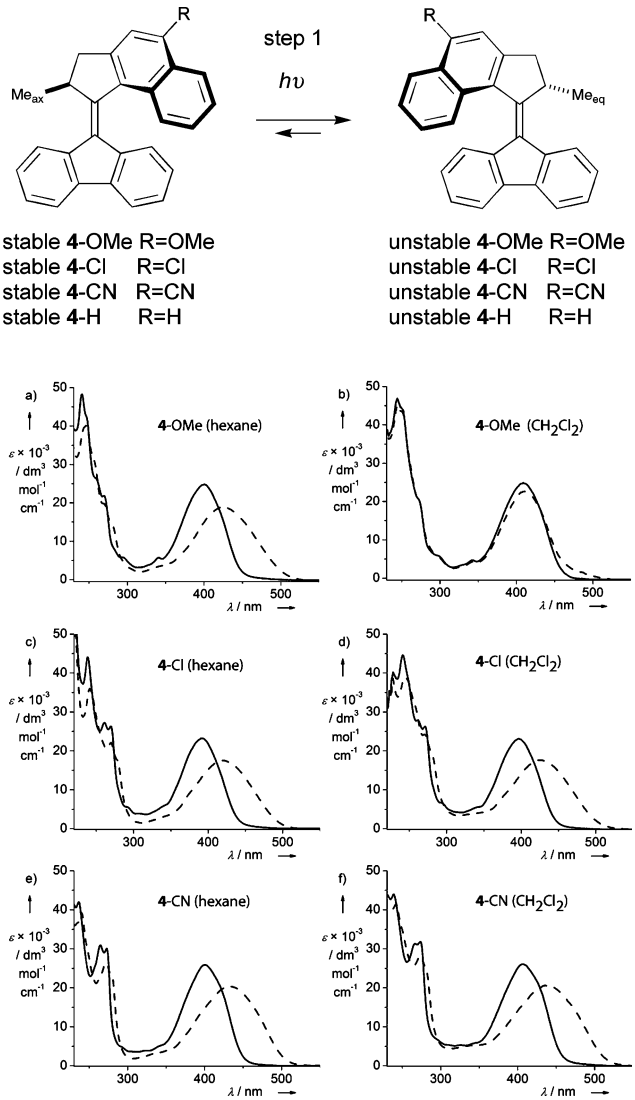


Fig. 6 UV–vis spectra of stable **4**-R (solid) and $PSS_{365\,nm}$ containing stable and unstable **4**-R (dashed) at −20 °C: (a) **4**-OMe in hexane, (b) **4**-OMe in CH_2Cl_2, (c) **4**-Cl in hexane, (d) **4**-Cl in CH_2Cl_2, (e) **4**-CN in hexane, (f) **4**-CN in CH_2Cl_2.

the unstable isomers are shifted downfield relative to the stable isomers (Fig. 7), as has been observed for **4**-H.[20]

This shift is consistent with the methyl group having changed from a pseudo-axial to a pseudo-equatorial conformation. Additionally, the absorption from the proton at the stereogenic center moved upfield, consistent with it changing from a pseudo-equatorial to a pseudo-axial conformation. By comparison of the relative integrals for these absorptions, we found that the photoequilibria of each of the alkenes are similar in toluene-d_8, with a slightly less favourable value observed for **4**-OMe (Table 1).

Irradiation of **4**-Cl, and **4**-CN in CD_2Cl_2 under identical conditions as described above gave similar photochemical behaviour and PSSs. However, we were unable to observe the formation of unstable **4**-OMe by ^{1}H NMR spectroscopy even after prolonged irradiation times, as might be expected from the results of the analysis described above employing UV–vis spectroscopy.

Table 1 Photoequilibria determined by ^{1}H NMR after irradiation at $\lambda = 365$ nm in toluene-d_8 and CD_2Cl_2 at −40 °C

Alkene	$PSS_{365\,nm}$ unst : st (tol-d_8)	$PSS_{365\,nm}$ unst : st (CD_2Cl_2)	Absorptions of $(CH_3)_{ax} \rightarrow (CH_3)_{eq}$ (ppm) in tol-d_8
4-OMe	57 : 43	< 2%[a]	1.23→1.48
4-Cl	70 : 30	85 : 15	1.05→1.36
4-CN	82 : 18	79 : 21	0.98→1.31
4-H	75 : 25	nd	1.11→1.40

[a] No unstable isomer was observed.

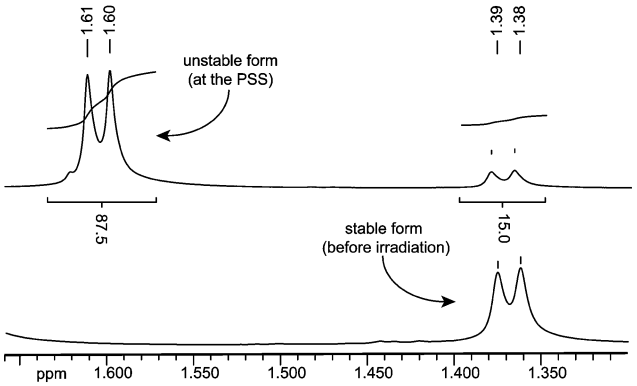


Fig. 7 Expansion of the ^{1}H NMR spectra (CD_2Cl_2) of **4**-Cl containing the absorptions from the methyl group at the stereogenic center, before irradiation (bottom) and at its $PSS_{365\,nm}$ (top).

Step 2: Thermal isomerisation

The thermal reversibility of all four alkenes, in both hexane and CH_2Cl_2, was confirmed by the regeneration of the original UV–vis spectra upon warming to rt for 20 min. These observations are consistent with the expected thermal helix inversion (step 2) of the unstable to the stable form, completing a 180° rotation of the upper-half relative to the lower-half.

To allow a quantitative comparison of each system, the thermal isomerisation steps of each of the motors were monitored by following the change in absorption at 445 nm with respect to time at four different temperatures (−10, 0, 10 and 20 °C). Using the different rate constants, the Gibbs free energy $\Delta^{\ddagger}G^{\circ}$ for the process was calculated by using the Eyring equation (data shown in Table 2 together with the $t_{1/2}$ at rt).

Comparison of the half-lives of the unstable isomers shows no significant differences, which suggests that the electron-donating or withdrawing nature of the substituent does not significantly influence the barrier to thermal isomerisation (Table 2). Comparison of the values of $\Delta^{\ddagger}G^{\circ}$ is consistent with this analysis.

Low temperature ^{1}H NMR analysis of step 2: The isomerisation of the unstable isomers to stable isomers

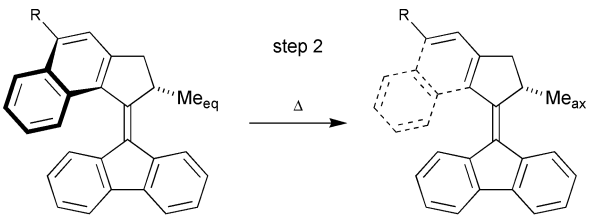
When the PSS samples in both toluene-d_8 or CD_2Cl_2 were allowed to warm to rt for 30 min, and were reanalysed by ^{1}H NMR spectroscopy, we found that the spectra showed a quantitative isomerisation of the unstable isomers back to the stable ones.

Conclusions

Here we demonstrate that molecular motors can be substituted with electron-withdrawing and donating substituents (R = Cl, CN, and OMe) in direct conjugation with the central double bond without significant influence on the rate-limiting, thermal isomerisation step of their rotary cycle. This indicates that in these systems, it is in fact predominantly steric factors that determine the barrier to the rate limiting thermal isomerisation step.

We also show that the photochemical step is quite sensitive to the combination of substituent and solvent. The striking effect of the solvent on quantum yield and photoequilibria for the methoxy

Table 2 Kinetic parameters for thermal helix inversion (step 2) of **4**-H, **4**-OMe, **4**-Cl and **4**-CN



unstable **4**-OMe R=OMe
unstable **4**-Cl R=Cl
unstable **4**-CN R=CN
unstable **4**-H R=H

stable **4**-OMe R=OMe
stable **4**-Cl R=Cl
stable **4**-CN R=CN
stable **4**-H R=H

Alkene	$\Delta^{\ddagger}G^{\circ}(kJ/mol)(hexane)$	$t_{1/2}$ at 20 °C in hexane (min)	$t_{1/2}$ at 20 °C in CH_2Cl_2 (min)
4-OMe R=OMe	86.6	5.2	4.7
4-Cl R=Cl	86.3	4.8	4.6
4-CN R=CN	86.4	4.9	4.3
4-H R=H	86.1	4.3	nd

substituted motor **4**-OMe alone suggests that apolar hydrocarbon solvents may be essential to the operation of some motors decorated with donor substituents. This knowledge will guide future efforts in the design of functionalised light-driven molecular motors, as well as the selection of appropriate conditions for their successful operation.

Experimental section

General remarks

Chemicals were purchased from Acros, Aldrich, Fluka or Merck. Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallised or distilled as necessary. Saturated solutions of $NaHCO_3$ and Na_2CO_3 were aqueous. Analytical TLC was performed with Merck SiO_2 gel 60 F254 plates and visualisation was accomplished by UV light. Flash chromatography was carried out using Merck SiO_2 gel 60 (230–400 mesh) according to the procedure of W. Clark Still *et al*.[40] NMR spectra were obtained using a Varian Mercury Plus and a Varian Unity Plus Varian-500, operating at 399.93 and 499.86 MHz, respectively, for the ^{1}H nucleus or at 100.57 and 125.70 MHz, respectively, for the ^{13}C nucleus. Chemical shifts are reported in δ units (ppm) relative to the residual deuterated solvent signals of $CHCl_3$ (^{1}H NMR: δ 7.26 ppm; ^{13}C NMR: δ 77.0 ppm). MS (EI) spectra were obtained with a Jeol JMS-600 spectrometer. UV–vis measurements were performed on a Hewlet-Packard HP 8543 FT spectrophotometer in conjunction with an JASCO PFD-350S/350L Peltier type FDCD attachment with a temperature control using Uvasol grade solvents (Merck). Irradiation experiments were performed with Spectroline model ENB-280C/FE lamp. Photostationary states (PSS) were ensured by monitoring changes in the sample composition in time by taking UV–vis spectra at −40 °C at distinct intervals until no further changes were observed. This was typically 20 min (for UV experiments) or 5 h (for ^{1}H NMR). Thermal helix inversions were monitored by UV–vis spectroscopy using the apparatus described above. A cutoff filter (350 nm) was used to minimise irradiation by the analysis lamp, as well as 20 s interval times for data point collection.

5-Methoxy-2-methyl-2,3-dihydro-1*H*-cyclopenta[*a*]naphthalen-1-one (7-OMe)

1-Methoxynaphthalene (1.58 g, 10.0 mmol) was added to mechanically stirred PPA (~80 mL) at 80 °C. After 5 min when mixing had occurred, methacrylic acid (0.86 g, 1.00 mmol) was added. The mixture was heated to 110 °C for 4 h. This mixture was cooled to 70 °C, and quenched by the addition of ice (50 g). This mixture was stirred for 3 h, and then extracted with EtOAc (4 × 50 mL), brine (20 mL), dried (Na_2SO_4) and concentrated *in vacuo*. This residue was purified by flash chromatography (SiO_2, heptane–EtOAc = 4 : 1) to give a light yellow solid. Recrystallisation from EtOH gave **7**-OMe as a white solid (0.972 g, 4.32 mmol, 43%): mp 134.0–135.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (d, J = 6.9 Hz, 3H, CH_3), 2.75–2.85 (m, 2H, CH_aH$_b$, CH), 3.42 (dd, J = 18.3, 8.0 Hz, 1H, CH$_a$$H_b$), 4.00 (s, 3H, OC$H_3$), 6.69 (s, 1H, Ar$H$), 7.46 (t, J = 7.7 Hz, 1H, ArH), 7.61 (t, J = 7.7 Hz, 1H, ArH), 8.19 (d, J = 8.4 Hz, 1H, ArH), 9.07 (d, J = 7.8 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 33.3, 39.7, 53.4, 99.0, 119.9, 120.9, 121.3, 122.6, 123.4, 126.7, 128.1, 156.7, 159.1, 205.9; HRMS (EI) calcd for $C_{15}H_{14}O_2$; 226.0994, found 226.1012.

5-Chloro-2,3-dihydro-2-methylcyclopenta[*a*]naphthalen-1-one (7-Cl)

1-Chloronaphthalene **6**-Cl (90% pure, 16.8 mL, 0.123 mol) was added to mechanically stirred polyphosphoric acid (200 g, 2.08 mol) at 80 °C. After 15 min, methacrylic acid (8.5 mL, 0.10 mol) was added slowly to the vigorously stirred emulsion. The mixture was stirred at 110 °C for 12 h. After cooling the reaction mixture to 70 °C, ice was added. The reaction flask was placed in an ice bath and water (75 mL) was added to the mixture and it was stirred for 2 h. The mixture was poured into a beaker and diluted with 500 mL of water. After stirring for another 4 h, the reaction mixture was extracted with ether (6 × 500 mL). The organic layers were washed with water (2 × 500 mL), saturated $NaHCO_3$ (1 × 1000 mL), brine (1 × 1000 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by column chromatography (SiO_2, heptane–toluene = 1 : 1, R_f = 0.14) and recrystallisation from methanol yielded a light brown solid (3.66 g, 15.9 mmol, 16%, 90% pure as judged by ^{1}H NMR. The impurity likely stems from the impurity in the commercial starting material 1-chloronaphthalene and could not be separated at this stage): mp 71.0–73.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.33 (d, J = 7.4 Hz, 3H, CH_3), 2.70 (dd, J = 21.6, 4.0 Hz, 1H, CH_2), 2.74 (m, 1H, CH), 3.34 (dd, J = 17.2, 7.6 Hz, 1H, CH_2), 7.48 (s, 1H, ArH), 7.61 (m, 2H, ArH), 8.20 (d, J = 8.4 Hz, 1H, ArH), 9.11 (d, J = 7.6 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 16.5, 34.9, 42.3, 124.1, 124.2, 124.6, 127.3, 129.0, 129.4, 129.7, 130.1, 139.7, 155.9, 208.8; HRMS (EI$^+$) calcd for $C_{14}H_{11}ClO$ 230.0498 found 230.0507.

2,3-Dihydro-2-methyl-1-oxo-1*H*-cyclopenta[*a*]naphthalene-5-carbonitrile (7-CN)

5-Chloro-2,3-dihydro-2-methylcyclopenta[*a*]naphthalen-1-one (**7**-Cl) (0.36 g, 1.6 mmol, corrected for the impurity in **7**-Cl), $Pd_2(dba)_3$ (2 mol%, 31 mg, 0.034 mmol), dppf (4 mol%, 38 mg, 0.069 mmol), Zn powder (12 mol%, 13 mg, 0.20 mmol) and $Zn(CN)_2$ (176 mg, 1.50 mmol) were placed in a flask and flushed with nitrogen. *N*,*N*-Dimethylacetamide (6 mL) was added and the mixture was heated at 120 °C for 12 h. The reaction mixture was cooled to room temperature, diluted with EtOAc (50 mL), washed with saturated Na_2CO_3 (4 × 30 mL), brine (1 × 30 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by column chromatography (SiO_2, pentane–EtOAc = 8 : 1→4 : 1, R_f = 0.52) and recrystallisation from methanol yielded **7**-CN as a light brown solid (276 mg, 1.25 mmol, 78%): mp 126.0–127.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.36 (d, J = 7.4 Hz, 3H, CH_3), 2.83 (m, 2H, CH and CH_aH$_b$), 3.49 (dd, J = 18.2, 8.2 Hz, 1H, CH$_a$$H_b$), 7.71 (m, 2H, Ar$H$), 7.89 (s, 1H, Ar$H$), 8.20 (d, J = 7.2 Hz, 1H, ArH), 9.14 (d, J = 8.8 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 15.9, 34.5, 42.3, 115.9, 116.6, 123.9, 124.8, 128.3, 128.4, 129.8, 130.1, 130.9, 133.0, 153.4, 208.6; HRMS (EI$^+$) calcd for $C_{15}H_{11}NO$ 221.0841 found 221.0832.

2,3-Dihydro-5-methoxy-2-methylcyclopenta[*a*]naphthalene-1-thione (9-OMe)

P_2S_5 (0.44 g, 1.0 mmol) was added to a stirred solution of 5-methoxy-2-methyl-2,3-dihydro-1*H*-cyclopenta[*a*]naphthalen-1-one (**7**-OMe) (0.23 g, 1.0 mmol) in benzene (30 mL). The mixture was then heated to reflux for 2 h, cooled to room temperature and the benzene was removed *in vacuo.* Purification by column chromatography (SiO_2, EtOAc–pentane = 1 : 16, R_f = 0.35) yielded a red solid (152 mg, 0.628 mmol, 63%): mp 64.0 °C (dec); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.47 (d, J = 7.2 Hz, 3H, CH_3), 2.88 (dd, J = 18.0, 2.4 Hz, 1H, CH_2), 3.10–3.20 (m, 1H, CH), 3.47 (dd, J = 18.4, 6.8 Hz, 1H, CH_2), 4.10 (s, 3H, OCH_3), 6.82 (s, 1H, ArH), 7.54 (m, 1H, ArH), 7.72 (m, 1H, ArH), 8.29 (d, J = 8.4 Hz, 1H, ArH), 10.17 (d, J = 8.4 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.9, 40.3, 54.8, 56.1, 101.1, 122.6, 124.2, 125.3, 126.2, 130.5, 131.3, 133.6, 162.0, 162.1, 245.0 ppm; HRMS (EI$^+$) calcd for $C_{15}H_{14}OS$ 242.0765 found 242.0776.

9-(2,3-Dihydro-5-methoxy-2-methylcyclopenta[*a*]naphthalen-1-ylidene)-9*H*-fluorenone (4-OMe)

9-Diazo-9*H*-fluorene (0.10 g, 0.52 mmol) was added to a stirred solution of **9**-OMe (0.10 g, 0.41 mmol) in benzene (30 mL). The reaction mixture was heated to reflux for 4 h, cooled to room temperature and the benzene was removed *in vacuo.* Purification by column chromatography (SiO_2, pentane–EtOAc = 16 : 1, R_f = 0.53), yielded a brown solid (0.11 g, 0.29 mmol, 71%): mp 191.0–193.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.39 (d, J = 6.4 Hz, 3H, CH_3), 2.71 (d, J = 15.2 Hz, 1H, CH_2), 3.55 (dd, J = 15.0, 5.8 Hz, 1H, CH_2), 4.10 (s, 3H, OCH_3), 4.31 (m, 1H, CH), 6.72 (d, J = 7.6 Hz, 1H, ArH), 6.80 (ABM, 1H, ArH), 6.94 (s, 1H, ArH), 7.18 (dt, J = 7.3, 1.1 Hz, 1H, ArH), 7.32 (m, 1H, ArH), 7.37 (m, 2H, ArH), 7.44 (m, 1H, ArH), 7.70 (d, J = 8.8 Hz, 1H, ArH), 7.76 (d, J = 7.6 Hz, 1H, ArH), 7.85 (m, 1H, ArH), 7.97 (m, 1H, ArH), 8.34 (d, J = 8.4 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.6, 42.5, 45.1, 55.8, 102.5, 118.8, 119.6, 122.7, 123.7, 124.6, 124.7, 125.7, 125.8, 126.3, 126.3, 126.7, 127.1, 127.3, 128.1, 128.6, 130.5, 137.2, 139.1, 139.7, 139.9, 149.2, 151.7, 158.0; HRMS (EI$^+$) calcd for $C_{28}H_{22}O$ 374.1671 found 374.1680.

9-(5-Chloro-2,3-dihydro-2-methylcyclopenta[*a*]naphthalen-1-ylidene)-9*H*-fluorenone (4-Cl)

P_2S_5 (0.44 g, 1.0 mmol) was added to a stirred solution of **7**-Cl (0.23 g, 1.0 mmol) in benzene (30 mL). The mixture was then heated to reflux for 2 h, the blue reaction mixture was cooled to room temperature and the benzene was removed *in vacuo.* The residue was dissolved in dichloromethane and filtered over SiO_2 (10 × 2 cm, pentane–EtOAc = 9 : 1), this yielded a green-blue crude solid product (0.2 g). P_2S_5 (0.90 g, 2.0 mmol) was added to a stirred solution of **7**-Cl (0.50 g, 2.2 mmol) in benzene (50 mL). After refluxing for 4 h the blue reaction mixture was cooled to room temperature. The reaction mixture was filtered through a SiO_2 plug, and eluted with benzene until the blue-green colour had completely eluted (10 mL) to give crude thioketone **9**-Cl. **9**-Cl was typically used without further purification. (Purification of **9**-Cl by chromatography for analysis was possible, but with a significant loss of product due to degradation on the column: (SiO_2, 9 : 1, hexane–EtOAc).) 5-Chloro-2,3-dihydro-2-methylcyclopenta[*a*]naphthalene-1-thione (**9**-Cl): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.47 (d, J = 7.2 Hz, 3H, CH_3), 2.86 (dd, J = 18.0, 2.4 Hz, 1H, CH_2), 3.12 (m, 1H, CH), 3.45 (dd, J = 18.2, 6.6 Hz, 1H, CH_2), 7.62 (s, 1H, ArH), 7.63 (m, 1H, ArH), 7.75 (m, 1H, ArH), 8.33 (d, J = 8.0 Hz, 1H, ArH), 10.12 (d, J = 7.6 Hz, 1H, ArH). 9-Diazo-9*H*-fluorene[23] (0.42 g, 2.2 mmol) was added to the filtrate and the mixture was heated at reflux for 4 h. After concentration *in vacuo*, purification by careful column chromatography (SiO_2, pentane–EtOAc = 50 : 1, R_f = 0.35) yielded a yellow solid (0.33 g), that appeared to be a mixture of alkene **4**-Cl and episulfide **10**-Cl. This mixture was dissolved in toluene (50 ml), treated with Ph_3P (2.0 g, 7.6 mmol) and heated to reflux for 12 h. After concentration *in vacuo*, purification by column chromatography (SiO_2, pentane–EtOAc = 50 : 1) yielded a yellow solid (0.25 g, 0.66 mmol, 30% from the ketone): mp 189.0–191.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.38 (d, J = 6.4 Hz, 3H, CH_3), 2.73 (d, J = 15.2 Hz, 1H, CH_2), 3.55 (dd, J = 15.2, 5.6 Hz, 1H, CH_2), 4.33 (apparent quin, J = 6.4 Hz, 1H, CH), 6.66 (d, J = 7.6 Hz, 1H, ArH), 6.78 (ABM, 1H, ArH), 7.21 (dt, J = 7.5, 1.1 Hz, 1H, ArH), 7.37 (m, 3H, ArH), 7.56 (m, 1H, ArH), 7.69 (s, 1H, ArH), 7.74 (d, J = 7.6 Hz, 1H, ArH), 7.83 (m, 2H, ArH), 7.95, 7.96–8.01 (m, 1H, ArH), 8.38 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.2, 41.8, 45.4, 119.0, 119.7, 124.1, 124.6, 125.1, 125.7, 126.0, 126.4, 127.0, 127.1, 127.2, 127.3, 127.9, 129.6, 130.6, 130.9, 134.1, 135.8, 136.9, 139.6, 139.7, 140.1, 147.1, 149.8; HRMS (EI$^+$) calcd for $C_{27}H_{19}Cl$ 378.1175 found 378.1189.

1-(9*H*-Fluoren-9-ylidene)-2,3-dihydro-2-methyl-1*H*-cyclopenta[*a*]naphthalene-5-carbonitrile (4-CN)

$Pd_2(dba)_3$ (4.8 mg, 0.0052 mmol, 2 mol%), dppf (6.7 mg, 0.012 mmol, 4 mol%), Zn powder (3.4 mg, 0.052 mmol, 19 mol%) and $Zn(CN)_2$ (66 mg, 0.56 mmol) were placed in a flask and flushed with nitrogen. A solution of **4**-Cl (105 mg, 0.278 mmol) in *N*,*N*-dimethylacetamide (6 mL) was added and the mixture was heated at 150 °C for 12 h. The reaction mixture was cooled to rt, diluted with EtOAc (50 mL), washed with saturated Na_2CO_3 (4 × 30 mL), brine (1 × 30 mL), dried (Na_2SO_4) and concentrated *in vacuo.* Purification by column chromatography (SiO_2, pentane–EtOAc = 16 : 1, R_f = 0.45) yielded a bright yellow solid (93 mg, 0.25 mmol, 90%): mp >221 °C (dec); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.36 (d, J = 7.2 Hz, 3H, CH_3), 2.78 (d, J = 15.2 Hz, 1H, CH_2), 3.57 (dd, J = 15.0, 5.2 Hz, 1H, CH_2), 4.35 (m, 1H, CH), 6.56 (d, J = 8.0 Hz, 1H, ArH), 6.76 (ABM, 1H, ArH), 7.20 (dt, J = 7.6, 0.8 Hz, 1H, ArH), 7.39 (m, 3H, ArH), 7.65 (m, 1H, ArH), 7.72 (d, J = 7.6 Hz, 1H, ArH), 7.81 (m, 1H, ArH), 7.88 (d, J = 8.8 Hz, 1H, ArH), 7.93 (m, 1H, ArH), 7.98 (s, 1H, ArH), 8.34 (d, J = 8.4 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.6, 41.4, 45.5, 111.2, 118.2, 119.2, 119.7, 124.4, 125.8, 125.9, 126.2, 127.3, 127.9, 127.9, 127.9, 127.9, 128.2, 129.3, 130.1, 131.9, 133.7, 136.6, 139.3, 140.1, 140.5, 142.1, 145.3, 148.2; HRMS (EI$^+$) calcd for $C_{28}H_{19}N$ 369.1518 found 369.1507.

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