Nanoscale Rotary Motors

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Controlled Rotary Motion in a Monolayer of Molecular Motors**

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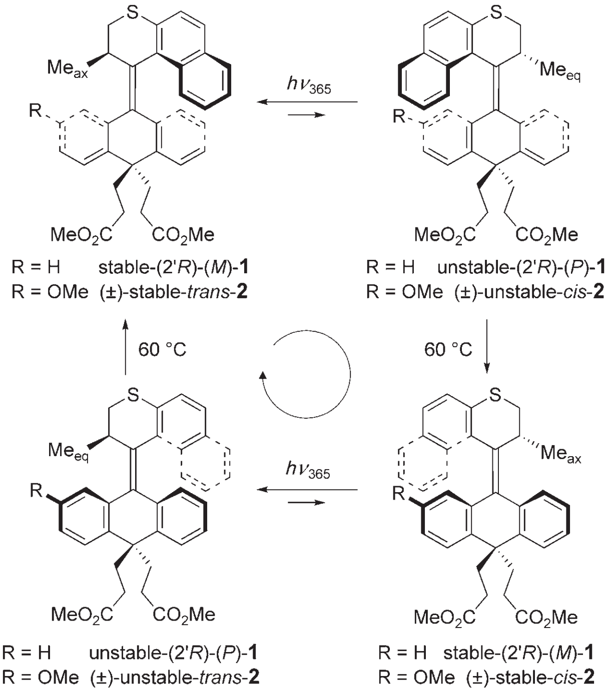
Rotary molecular motors are ubiquitous in natural systems where they are used for diverse tasks including molecular transport, cellular translocation, and ATP synthesis, and are considered key components of future synthetic nanomechanical devices.[1,2] In many of these systems, such as ATPase or the bacterial flagella motor, immobilization into the cellular membrane allows their rotary action to be harnessed. Attaching biological or synthetic molecular rotary motors to solid substrates is considered to be a key step toward the fabrication of devices that exploit the collective rotational mechanical motion generated by these systems.[3,4] Although linear synthetic[5,6] and biological motors[2,7] have been mounted on surfaces, examples of surface-bound rotary motors are scarce.[2,8,9] Preliminary work to this end includes the successful characterization of functioning ATPase while immobilized on quartz[8] and recently, a single example of synthetic rotary molecular motors functioning on gold nanoparticles in solution.[9] Although the latter is a significant step toward future applications, the nanoparticles in solution are still overwhelmed by Brownian rotation and translation, and the motor function might to some extent suffer from excited-state quenching by the gold, making it difficult to harness work from the system.

Herein we present the transformation of the relative unidirectional rotation of the two halves of a synthetic rotary molecular motor in solution into the controlled azimuthal rotary motion of the upper half of the motor molecule relative to the lower half, which is grafted to a quartz surface. The photochemical and thermal behavior of the motor in the monolayer was correlated to its counterpart in solution by using CD spectroscopy. X-ray photoelectron spectroscopy (XPS) was employed to verify that the lower (stator) half of the molecules was grafted to the surface through two points of attachment, thus preventing Brownian rotation of the motor molecules.

A modified 2nd generation enantiopure light-driven molecular motor[10] (**1**, Scheme 1) was synthesized[11] with the lower half "stator" of the molecule functionalized with two ester moieties to facilitate its attachment to a surface. The stable isomer of motor molecule **1** possesses a single stereogenic center bearing a methyl group that dictates the direction of rotation, and which adopts a pseudoaxial conformation to minimize steric strain. The motor functions by absorption of a photon (energy input) leading to a *cis*→*trans* isomerization of the central double bond, which is the motor's axis of rotation. This isomerization leaves the molecule in a high-energy conformation in which the methyl group adopts a pseudoequatorial orientation where it experiences steric crowding with the lower half of the molecule. A thermodynamically favorable helix inversion relieves the strain as both the methyl group and the naphthalene ring slip past the aromatic moieties of the lower half, regenerating the stable conformation with a pseudoaxial methyl group and finishing 180° of rotation. Repeating this cycle results in a complete 360° unidirectional rotation.

The kinetics of the thermal helix inversion during conversion of unstable-(2′*R*)-(*P*)-**1** to stable-(2′*R*)-(*M*)-**1** in



Scheme 1. Four-step rotary cycle of **1** and **2**.

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heptane solution (for CD spectra, see Figure 1) were determined by monitoring the change in CD intensity with respect to time at four different temperatures ($T = 323$, 333, 343, 353 K). By using the Eyring equation, it was determined that the Gibbs free energy of activation was $\Delta^{\ddagger}G^{\circ} = 26.0$ kcal mol^{-1}, indicating slow helix inversion at room temperature. ^{1}H NMR spectroscopic analysis of a sample of racemic stable-**1** after photoirradiation in [D$_6$]benzene revealed that the photostationary state at 365 nm (PSS$_{365}$) contained a 4.5:1 ratio of unstable to stable isomers.

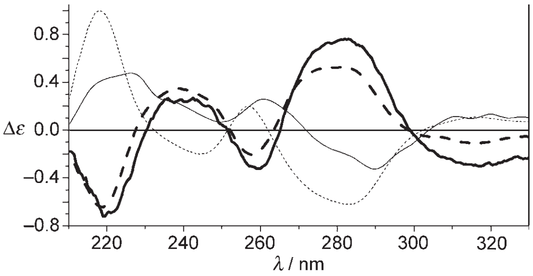
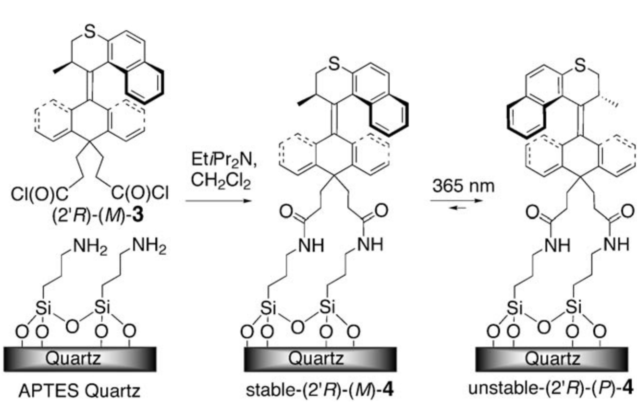


Figure 1. CD spectra of stable-(2′*R*)-(*M*)-**1** (dashed line) and the PSS$_{365}$ of unstable-(2′*R*)-(*P*)-**1** (bold dashed line; both in heptane), and of surface grafted stable-(2′*R*)-(*M*)-**4** (solid line) and a PSS$_{365}$ of unstable-(2′*R*)-(*P*)-**4** (bold solid line). The magnitude of the solution CD spectra were adjusted for comparison.[11]

To verify that this molecule functions as a rotary molecular motor analogous to known systems,[10] compound **2** bearing a methoxy substituent was prepared. Irradiation ($\lambda = 365$ nm) of stable-*cis*-**2** resulted in its conversion to unstable-*trans*-**2**, which converted into stable-*trans*-**2** upon warming to 60 °C for 3 h. Under conditions in which no thermal isomerization occurs, a secondary, slower photochemical side process was also observed in which stable-*cis*-**2** isomerized directly to stable-*trans*-**2**. ^{1}H NMR spectroscopic analysis of the molar ratio of the isomers during the irradiation of stable-*cis*-**2** revealed that the conversion of stable-*cis*-**2** to the unstable-*trans*-**2** occurs five times faster than to stable-*trans*-**2**.[11,12]

Quartz was selected as the surface to minimize Brownian motion of the system and because it should allow UV and CD analysis of the system[13] and not interfere with any photochemical processes required for successful operation of the motor. To immobilize the motor on a surface, quartz plates coated with 3-aminopropyltriethoxysilane (APTES)[14] were functionalized with (2′*R*)-(*M*)-**3** by immersing the plates into a 0.01 M CH_2Cl_2 solution of the diacid chloride in the presence of Hünig's base for 24 h then rinsing and sonicating the sample in CH_2Cl_2 then MeOH to give stable-(2′*R*)-(*M*)-**4** (Scheme 2).

The CD spectrum of the monolayer clearly shows the presence of surface-bound motor (2′*R*)-(*M*)-**4** (Figure 1), which is similar in profile to (2′*R*)-(*M*)-**1** in solution. In contrast to typical solution experiments, however, **4** isomerizes to its unstable isomer to some extent under the influence of the light of the CD spectrometer.[15] To address this, the CD of the stable isomer was recorded at 80 °C so that fewer scans were necessary.[16]



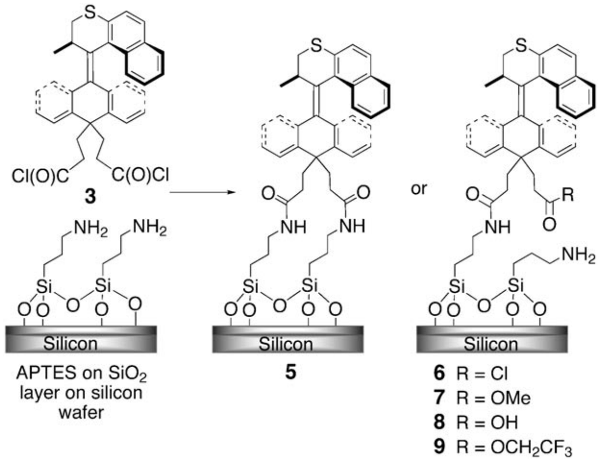
Scheme 2. Grafting (2′*R*)-(*M*)-**3** to APTES-modified quartz.

Irradiation of stable-(2′*R*)-(*M*)-**4** with UV light ($\lambda = 365$ nm) for 15 min under an N_2 atmosphere caused an inversion of the major bands of the CD spectrum (Figure 1, solid and bold lines) in analogy with the spectral inversion observed after irradiation of (2′*R*)-(*M*)-**1** in solution. This is indicative of the photoisomerization of stable-(2′*R*)-(M)-**4** to unstable-(2′*R*)-(*P*)-**4**. Moreover, subsequent heating of the sample resulted in nearly complete regeneration of the original CD spectrum. By analogy with the CD studies performed on the parent motors **1** and **2** in solution, from these data we assume that **4** retains its function as unidirectional rotary molecular motor.

To transform the relative unidirectional rotation of the upper-half "rotor" relative to the lower-half "stator" into the controlled rotation of the rotor with respect to the surface, the uncontrolled Brownian rotation of the motor molecule must be prevented by grafting it to the surface through two points as in **4** (Scheme 2). The successful reaction of both acid chloride moieties of **3** with two surface-bound amines was verified by XPS spectroscopy.[17] As XPS data were required for quantitative analysis, surface charging was minimized by performing the analysis on a motor monolayer immobilized on a 10-nm oxidized layer on a silicon wafer. The silicon-bound APTES monolayer was prepared in a manner analogous to the quartz substrate.[11,18]

Grafting motor **3** to the monolayer by reaction of the surface amines with both of the acid chlorides generates the desired diamide (**5**, Scheme 3), whereas reaction of only one of the acid chlorides would leave one acid chloride remaining (**6**, Scheme 3). If present, this reactive function is converted with MeOH or moisture during workup A to give **7** or **8**, respectively, or 2,2,2-trifluoroethyl ester **9** during workup B (Scheme 3). XPS analysis of the modified surface allows the differentiation of each of these species. When either workup procedure was used, quantitative comparison of the sulphur 2p photoemission line (164.0 eV), originating from the thioether sulphur,[19] with the respective N 1s photoemission from the amide nitrogen (399.6 eV) showed a 1:2 ratio.[11]

Cross-comparison of the ratio between the peak area caused by the amide carbonyl carbon NH*C*(O) (288.2 eV) and the amide nitrogen *N*HC(O) is 1:1, which is also consistent with the expected ratios for the formation of **5**. The formation of **6**, **7**, and **8** was not observed as no signal was



Scheme 3. Schematic diagram showing **3** being grafted to an amine monolayer on a surface-oxidized silicon wafer for XPS analysis. Compound **5** was generated without any detectable amounts of **6**–**9** (see text for explanation).

detected in the 2p photoemission spectrum of chlorine (200.0–202.0 eV) or from the carbonyl carbon of esters (288.8 eV) or carboxylic acids (289.6 eV) in the 1s spectrum of carbon (Figure 2) when either workup procedure was used.[15]

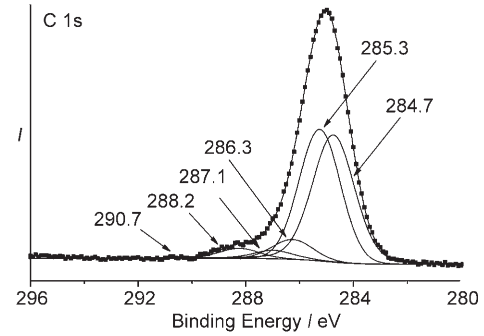


Figure 2. Photoemission spectra fit (——) to the experimental data (■) of the C 1s core-level region of **5**. The take-off angle used was 37°.

When workup B with trifluoroethanol and catalytic 4-dimethylaminopyridine (DMAP) was used, no fluorine signal (688.0–690.0 eV) was observed. This is also consistent with the successful formation of **5** and not **9**. Collectively, these data are consistent with greater than 90% of the motor molecules being attached to the surface through two amide bonds.

In conclusion, by correlating the CD spectroscopic behavior of molecular motors in a monolayer on quartz with its counterpart in solution, we show that these systems function while attached to a quartz substrate. This should result in the conversion of the relative rotary action in solution into the absolute rotation of the rotor-half relative to the surface. This may prove to be a crucial step toward harnessing work from these motors by collective action and provides the basis for the development of these systems for single molecule analysis.

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[11] See the Supporting Information.

[12] Continued irradiation ultimately gave a photostationary state containing all four isomers of **2** in a 40:43:9:8 ratio of unstable-*cis*/unstable-*trans*/stable-*cis*/stable-*trans*, respectively.

[13] To the best of our knowledge, this is the first CD spectrum reported of a covalently grafted monolayer of small molecules. A CD spectrum of a Langmuir–Blodgett monolayer has been reported, see: C. Nuckolls, T. J. Katz, T. Verbiest, S. V. Elshocht, H.-G. Kuball, S. Kiesewalter, A. J. Lovinger, A. Persoons, *J. Am. Chem. Soc.* **1998**, *120*, 8656–8660.

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[15] See the Supporting Information for quantification of this effect.

[16] The curve for the stable form was smoothed owing to the poorer signal-to-noise ratio.

[17] XPS was recently used to estimate the number of attached tethers of a polyolefin to silicon, see: C. M. Yam, J. Cho, C. Cai, *Langmuir* **2004**, *20*, 1228–1233.

[18] By using XPS and data from reference [14], we estimated the surface coverage be approximately 1 motor/8 nm^2.

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