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A Generic Basis for Some Simple Light-Operated Mechanical Molecular Machines

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The widespread utilization of submolecular motion in key biological processes is inspiring scientists to try to bridge the gap between synthetic chemical systems, which, by and large, rely upon electronic and chemical effects and do not exploit molecular-level motion (a notable exception being liquid crystals), and the macroscopic world, where our everyday machines rely upon the controlled movement of multiple components to perform specific tasks. Most efforts toward this goal have focused on establishing methods (for example, the use of light) to control the positioning or movement of submolecular fragments,[1] but relatively little attention[2] has been given to what the effects of such motion might be. A bi-stable [2]-rotaxane (a "molecular shuttle") was recently described in which a macrocycle could be moved with great positional integrity between two well-separated binding sites in response to a photostimulus.[3,4] Here we show how this large positional change can be used to create a light-activated switch for fluorescence, exhibiting an exceptional 200:1 on−off intensity ratio between the translational states (~85:1 between the photostationary state and the *cis*-isomer).[5] We suggest that such "mechanical switching" could form the basis for many different types of synthetic property-changing devices and materials that, like biological systems, function through mechanical motion at the molecular level (Figure 1).

Molecular shuttle *E*/*Z*-**1** (Scheme 1) has several key features: A fumaramide−maleamide unit (dark blue−pink) provides a means of changing the position of the macrocycle on the thread by altering the binding affinity of one station for the macrocycle by several kilocalories per mole using various olefin isomerization reactions (photochemical, chemical, or thermal).[3] A glycylglycine unit (orange) offers a nonreactive station of intermediate binding affinity between fumaramide and maleamide.[2c] The spacer between the stations, here a C_{11} alkyl chain, can be chosen to suit the distance dependency of the property one wishes to influence. Here we illustrate the concept using fluorescence, introduced by attaching a 9-carboxyanthracene residue (which is sufficiently bulky to also act as a "stopper") to the peptide station. The macrocycle contains two pyridinium units, which are known to quench anthracene fluorescence through electron transfer.[6] Since electron transfer can sometimes be remarkably efficient over long distances, we carried out INDO/S calculations (see Supporting Information) to confirm that the quenching should have the required high distance and orientation dependency in *E*/*Z*-**1**.

Rotaxane *E*-**1** was prepared in 48% yield from thread *E*-**2** and converted into *Z*-**1** by photoisomerization (Scheme 1). The ^{1}H NMR of *Z*-**1** in $CDCl_3$[7] (Figure 2) confirms the location of the macrocycle to be predominantly over the GlyGly residue. H_g and H_i are shielded by 0.6 and 0.8 ppm with respect to their position in *Z*-**2**, and no significant shifts are observed for $H_{o'}$ or $H_{p'}$. In contrast, in *E*-**1** the macrocycle resides overwhelmingly over the fumaramide station.

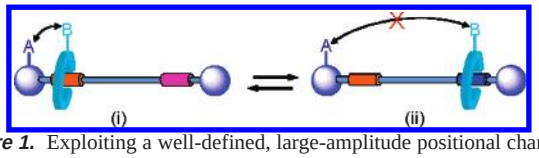
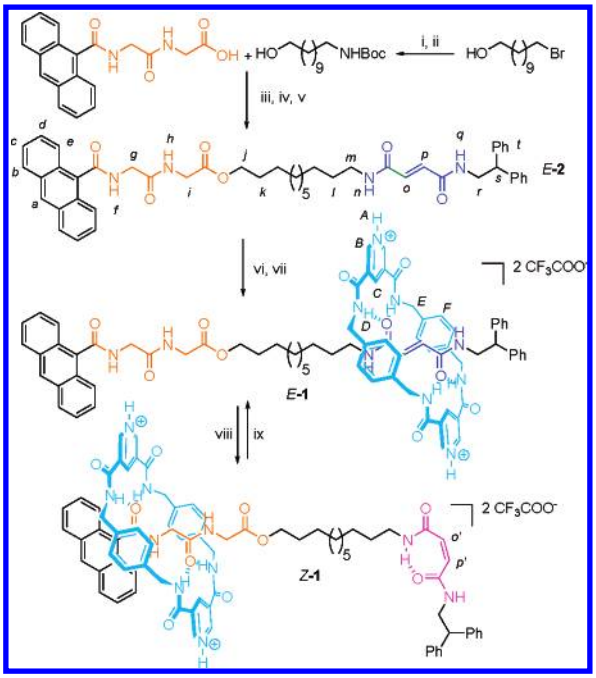


Figure 1. Exploiting a well-defined, large-amplitude positional change to trigger property changes. (i) A and B interact to produce a physical response (fluorescence quenching, specific dipole or magnetic moment, NLO properties, color, creation/concealment of a binding site or reactive/catalytic group, hydrophobic/hydrophilic region, etc.); (ii) moving A and B far apart mechanically switches off the interaction and the corresponding property effect.

Scheme 1. Synthesis of Molecular Shuttle *E*/*Z*-**1**[a]



[a] Reaction conditions: (i) potassium phthalimide, DMF, 80 °C, 16 h, 98%; (ii) $NH_2NH_2{\cdot}H_2O$, EtOH, reflux, 1 h, then $(Boc)_2O$, KOH, MeOH, ~100%; (iii) 1-[3-dimethylaminopropyl]-3-ethylcarbodiimide hydrochloride (EDCI), 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, 60%; (iv) trifluoroacetic acid (TFA), CH_2Cl_2; (v) EDCI, DMAP, CH_2Cl_2/DMF, (*E*)-3-(2,2-diphenylethylcarbamoyl)acrylic acid 60%; (vi) 3,5-pyridinedicarbonyl dichloride, *p*-xylylenediamine, Et_3N, $CHCl_3$, 48%; (vii) TFA, CH_2Cl_2; (viii) 312 nm, CH_2Cl_2, 20 min, 60%; (ix) 312 nm, CH_2Cl_2, 20 min, 40%, or piperidine (3 equiv), CH_2Cl_2, rt, 16 h ~100% or $C_2H_2Cl_4$, 115 °C, 2 days, 90%. *Z*-**2** is the *cis*-olefin isomer of *E*-**2**, its chemical structure is formally provided in the SI.

H_o and H_p are shifted 1.1 ppm upfield with respect to their positions in the thread, while H_i and H_g occur at identical chemical shifts in rotaxane and thread. The ^{1}H NMR signal for H_A and the significant shifts in the pyridine signals compared to the free base rotaxanes (see SI) confirm the protonation of the pyridine rings.

The photostationary state (PSS) of *E*-**1**/*Z*-**1** (or *E*-**2**/*Z*-**2**) at 312 nm in CH_2Cl_2 is 40:60 (electronic absorption spectra are provided

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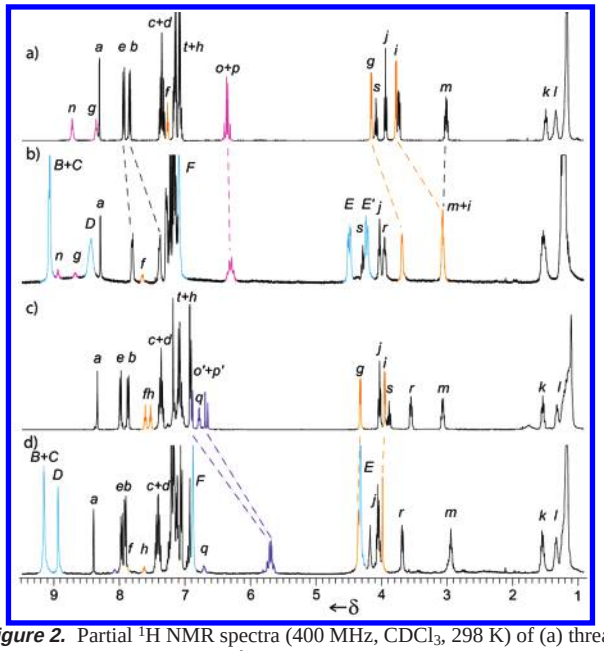

Figure 2. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of (a) thread *Z*-**2**, (b) [2]rotaxane *Z*-**1** (H_A $\delta = 13.36$ ppm), (c) thread *E*-**2**, and (d) [2]-rotaxane *E*-**1** (H_A $\delta = 13.45$ ppm). All samples contained 2 equiv of CF_3-COOH. The assignments correspond to the lettering shown in Scheme 1.

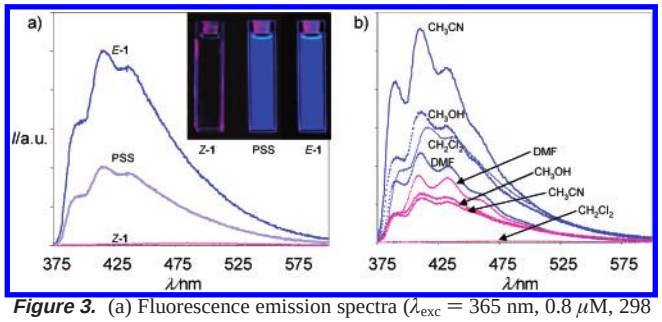

Figure 3. (a) Fluorescence emission spectra ($\lambda_{exc} = 365$ nm, 0.8 μM, 298 K) of *E*-**1** (blue), *Z*-**1** (pink), and the photostationary state (PSS, mauve). The difference in fluorescence intensity between *Z*-**1** and *E*-**1** or the PSS is clearly visible to the naked eye (inset: picture of the cuvettes under 365 nm UV light). (b) Fluorescence emission spectra ($\lambda_{exc} = 365$ nm, 0.8 μM, 298 K) of *E*-**1** (blue) and *Z*-**1** (pink) in each of CH_2Cl_2, CH_3CN, CH_3OH, and DMF. All the experiments were carried out after the addition of 2 equiv of CF_3COOH (TFA). Similar quenching and red-shifting was observed for the bis(methylpyridinium tetrafluoroborate) analogue of *Z*-**1** ((i) *Z*-**1**, MeI, CH_3CN, (ii) $AgBF_4$). In the absence of TFA, *E*-**1** and *Z*-**1** exhibit fluorescence spectra similar to those of the corresponding isophthalamide macrocycle-based rotaxanes (i.e. nonquenched and, for *Z*-**1**, broadened and red-shifted).[4d] In contrast, both threads (*E*/*Z*-**2**) have fluorescence spectra indistinguishable from those of anthracene 9-carboxyamide and are unaffected by the addition of TFA.

in the Supporting Information) and, starting from either isomer, is reached within 20 min with no evidence of any decomposition.

Fluorescence spectra ($\lambda_{exc} = 365$ nm) were obtained from 0.8 μM solutions of *E*-**1** and *Z*-**1** in CH_2Cl_2, CH_3CN, CH_3OH, and DMF (Figure 3). A remarkable 200:1 intensity ratio between the trans and cis shuttles (~85:1 between *Z*-**1** and the PSS) is observed for the CH_2Cl_2 solutions at the maximum of *E*-**1** emission ($\lambda_{max} = 417$ nm), *Z*-**1**'s fluorescence being almost completely quenched by the pyridinium units and strongly red-shifted (Supporting Information) by intercomponent hydrogen bonding of the anthracene carboxyamide group to the macrocycle.[4d,8,9] The emission spectra in the various solvents show an *increase* in *Z*-**1** luminescence with increasing hydrogen bond basicity[10] ($CH_2Cl_2 < CH_3CN < CH_3OH <$ DMF), consistent with a reduction in positional integrity of the macrocycle at the GlyGly station as the intercomponent hydrogen bonds are weakened. Conversely, the fluorescence intensity of *E*-**1** generally *decreases* with this trend (opposite to the normally observed polarity effects on electron transfer and excited-state relaxation processes) as the macrocycle increasingly spends time away from the fumaramide station in positions within efficient quenching distance of the anthracene. The exception, the reduced fluorescence intensity of *E*-**1** in CH_2Cl_2 compared to that in CH_3CN and CH_3OH, is presumably a result of some H-bond-induced intramolecular folding.

The bi-stability and integrity of the macrocycle positioning in CH_2Cl_2 means that starting with pure *Z*-**1** (the "off" state) the system can be written with light at 312 nm to give a photostationary *E*/*Z*-**1** state which emits ~85 times more light than the starting material when addressed at a remote wavelength ($\lambda_{exc} = 365$ nm).[11] Once written, it is essentially stable ($T_{1/2} \approx 24$ h at 115 °C) unless treated with piperidine. The most important feature of the system, however, is that it demonstrates a principle which could be used to make switches that can change *any* property that can be made to depend on the spatial separation of submolecular fragments (Figure 1). The use of stimuli-induced motion to bring individual components together to perform specific tasks (e.g. electron transfer from one part to another) which produce an effect (e.g., fluorescence quenching), arguably makes such structures true mechanical molecular machines.

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Supporting Information Available: Synthetic experimental procedures and INDO/S calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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